Thesis for the Degree of Ph.D.

I. The Transmission of Polarity Effects through Singly Bound Carbon Atoms

and

2. The Influence of Substituent Groups on the Course of Etard's Reaction.

by

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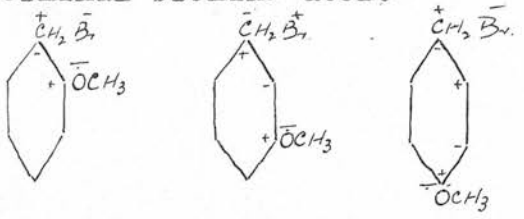
Within recent years investigators have been endeavouring to formulate theories to explain the mode of reactivity of organic compounds. A new chapter in this field of investigation has been opened up by the attempts made by various chemists to explain reactivity on an electronic basis. The important contributions by Robinson (Mem.Manchester Phil.Soc. I920 64 No.4) Vorlander (Ber. I9I9 52 263) and Lapworth (Mem.Manchester Phil.Soc. I920 No.3) in this connection are of particular value. The theory advanced by Lapworth has perhaps created most discussion. He formulated a principle on induced alternate polarities and by its aid it was possible to explain and predict both molecular reactivity and non reactivity. It had the fundamental idea that the carbon atoms in a ring or chain could be made to exhibit an alternating polarity which made itself apparent in differences in reactivity of atoms influenced by a "key atom" at a distance from them. The influence passes readily along a conjugated chain of carbon atoms, or through the conjugated system present in benzene, or even through a limited number of single bonds.

Investigations have been carried out by several chemists on substituted benzene derivatives in which a strongly positive group such as COOH, NO_2 or a strongly negative/

negative group such as OCH_3, CH_3, Cl etc., has been introduced into the molecule and as the effect on the reactivity of the atoms in the molecule examined. Lapworth and Shoesmith (J. 1922 121 1391) have obtained a striking example of induced polar effects in the isomeric methoxy benzyl bromides. The oxygen of the methoxyl group here acts as the "key atom" and it was shown that an induced alternate polarity was set up in the molecule which made itself apparent in the character of the terminal bromine atom.



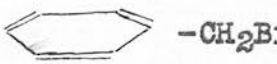
Thus the tendency of the key atom is to make the bromine more negative in character in the ortho and para compounds and more positive in the meta compound. This was found to be the case in the rapid hydrolysis of the ortho and para methoxy benzyl bromides as compared with the meta compound. A reversal of these results was obtained when the positive nature of the bromine atom was compared by the reduction of the compound with HI.

In the same manner Shoesmith and Slater (J. 125 1924 2278) have investigated the isomeric w bromxylenes. They proved that the methyl group exerts a considerable influence on the side chain halogen atom in virtue of the positive hydrogen atoms which it contains which act/

act as "key atoms". The bromine atom in the ω brom xylenes is thus induced negatively in the ortho and para compounds and ought to be hydrolysed more readily than the meta compound in consequence. The order of hydrolysis was found to be in agreement with this and there was a reversal of this order on reduction, i.e. meta > ortho and para.

A reversal of this order of reduction again was obtained by bringing the halogen one place nearer to the "key atom" as in the iodo toluenes. The halogen was induced positively in the ortho and para compounds and thus the order of reduction was ortho and para > meta.

Lowry (J. 1923 123 824) put forward a suggestion that the induced alternate influence is only experienced in a perfect system of conjugated double bonds. This has been entirely negatived in the w brom-xylenes but it is ~~an~~ interesting at this stage to enquire how far the inducing effect of a "key atom" would extend in a side chain which contains a series of consecutive single bonds. This problem would be solved by examining compounds in which the halogen atom is one place further from the benzene nucleus than in the substituted benzyl bromides i.e. compounds of the general type X -  $-CH_2-$ CH_2-Br in which X is the "key atom". The other possibility would be to remove the key atom one place from the benzene nucleus as/

as in a compound of the type X - CH_2-  -CH_2Br but experience has shown that such groups as X - CH_2- really assume the influence of a CH_3 group.

Recently several investigators have been examining the directive action of such groups as -CH_2 NH_2 and -$CH_2CH_2NH_2$ on aromatic substitution. Goss, Hanhart and Ingold (J. 1927 250) have investigated the nitration of β phenylethylamine derivatives and compared the percentage of meta substituent isolated with the results of Goss Ingold and Wilson (J. 1926 2440) who nitrated benzylamine derivatives.

Their work is an attempt to elucidate the same problem as is occupying this research by determining to what extent the directing influence of basic groups separated from the benzene nucleus by one or more methylene groups is experienced in the meta substitution of a nitro group. The percentage of the meta nitro compound in each series determines the strength of the directing influence.

The following table (Goss, Hanhart, and Ingold, loc.cit.) will suffice to show how the directing influence of the basic group in weakened as the side chain is extended.

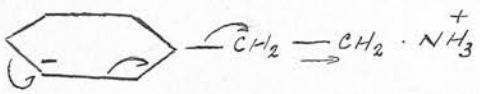
Nitration/

Nitration in HNO_3 (D I.5) at -10° to 0°

Benzylamine bases. Side chain	Proportion of m. substituent.	β phenylethylamine bases. Side chain	Proportion of m. substituent.
$-CH_2NH_2$	49%	$-CH_2-CH_2NH_2$	I2%
$-CH_2NMe$	69%	$-CH_2-CH_2NMe$	I5%
$-CH_2NMe_2$	58%	$-CH_2-CH_2NMe_2$	I3%
$-CH_2NMe_3$	88%	$-CH_2-CH_2NMe_3$	I9%

It will be shown how these results coincide completely with an entirely independent method of attacking the problem.

The work of these investigators is entirely confined to the capacity displayed by the terminal ammonium group $-\overset{+}{N}R_4$ to act as an attractor of electrons, thus leaving the meta position of the benzene ring negatively charged and hence the position of attack in substitution i.e.



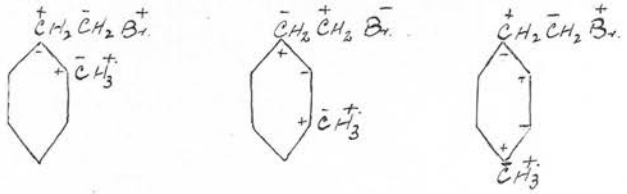
But in this way only a "general effect" of electron pull can be investigated.

This present investigation seeks to demonstrate the effect of an electron movement, started at one point in the benzene ring, when passed through the ring and then through a side chain containing two carbon atoms.

The/

The compounds which were obviously the most interesting for this investigation were the isomeric methoxy β phenyl ethyl bromides eg. OCH_3⟨⟩CH_2-CH_2Br and attempts were made to prepare these compounds. The corresponding alcohols were obtained in the pure state but an extraordinary difficulty was experienced in their bromination. The only reagent whoch would convert the corresponding methoxy alcohol to the bromide was PBr_5 but unfortunately at the same time it brought about nuclear bromination in the case of the ortho and meta compounds to too great an extent to permit of isolating the bromide in approximate purity.

However, the isomeric β tolyl ethyl bromides eg. CH_3⟨⟩$-CH_2-CH_2Br$ were obtained in the pure state and examinations of the rate of hydrolysis and reduction were carried out. From the theoretical considerations of the isomeric β tolyl ethyl bromides in which the hydrogen atoms of the methyl group are the "key atoms" it would be anticipated that if any induced polarity extended through the side chain the terminal Br atom w would be induced positively in the ortho and para isomers and negatively in the meta isomer.



i.e. the order of reactivity on hydrolysis ought to be meta/

meta > ortho and para. If any reduction took place which from comparison with the w bromxylenes was unlikely then a reversal of this order would be anticipated. This series was also compared with the unsubstituted compound β phenyl ethyl bromide.

The results of hydrolysis and reduction of these compounds led to some striking observations.

Hydrolysis.

I) There was no appreciable hydrolysis in aqueous alcohol over a period of four hours at 61°. A comparison with the w bromxylenes which are almost completely hydrolysed in aqueous alcohol at 61° at the end of three hours, serves to indicate how remarkably less active a Br atom one place further removed from the benzenoid nucleus than the w bromxylenes has become towards hydrolysing agents.

Aqueous alcoholic NaOH was required to effect a hydrolysis which was not complete after six hours at 76°.

2) The rate of hydrolysis of the unsubstituted compound β phenyl ethyl bromide is appreciably greater than the substituted compounds, which is a remarkable fact when one reviews the w bromxylenes in which benzyl bromide is appreciably slower in its rate of hydrolysis.

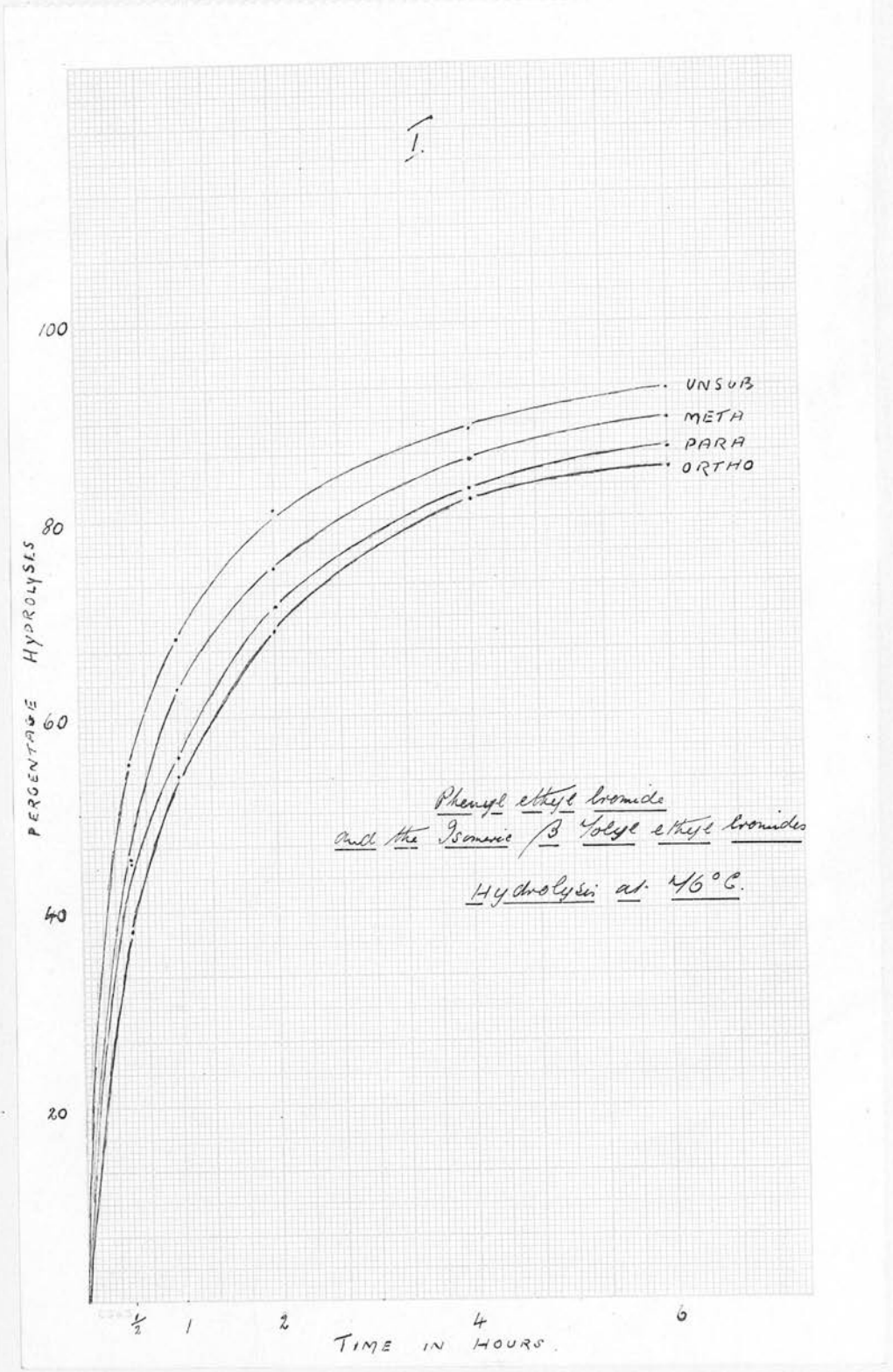
3) There is only a slight residuum of induced alternate polarity evident in the differences in the rates of hydrolysis in the isomeric β tolyl ethyl/

ethyl bromides. The order of reactivity is as anticipated from theoretical considerations i.e. meta > ortho and para, but it will be seen from a comparison of the following two graphs (I and II) of the hydrolysis curves of the β tolyl ethyl bromides and the w brom xylenes, the remarkable variations in the differences in the rates of hydrolysis and the two series as evidenced by the spacings between the curves in the two series. This shows clearly the loss of alternate polar effects across single bonds.

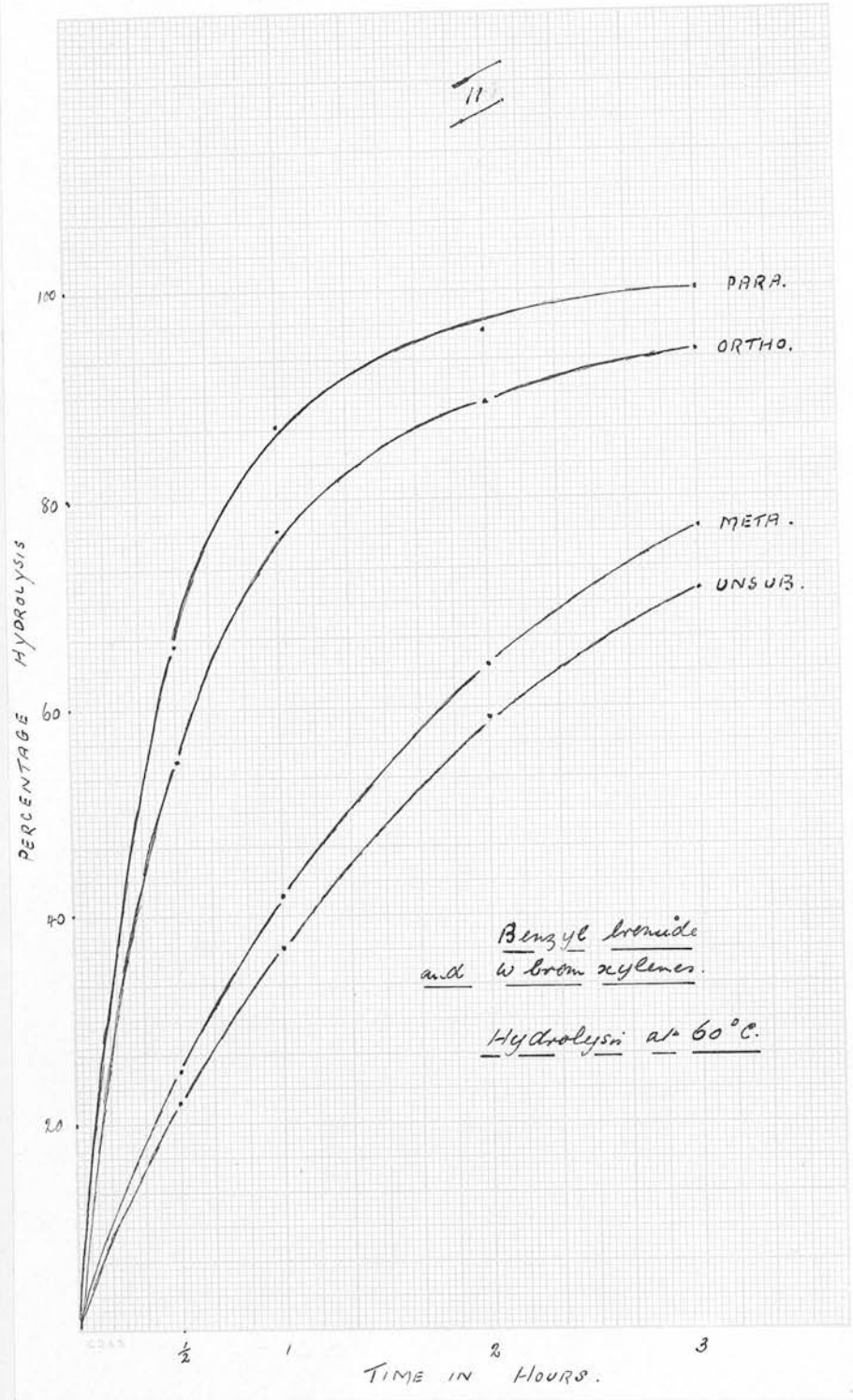
The two series were hydrolysed under different conditions. The tolyl ethyl bromides required aqueous alcoholic NaOH at 76° and the w brom-xylenes were hydrolysed by aqueous alcohol at 61° C.

P methoxy β phenyl ethyl bromide, which was the only isomer of this series obtained in a state approximately pure, was hydrolysed in a similar manner to the β tolyl ethyl bromide series and the results indicate the parallelism which was anticipated in the two series. Its hydrolysis curves along with those of β phenyl ethyl bromide and β p. tolyl ethyl bromide which are repeated for comparison purposes are given in graph III.

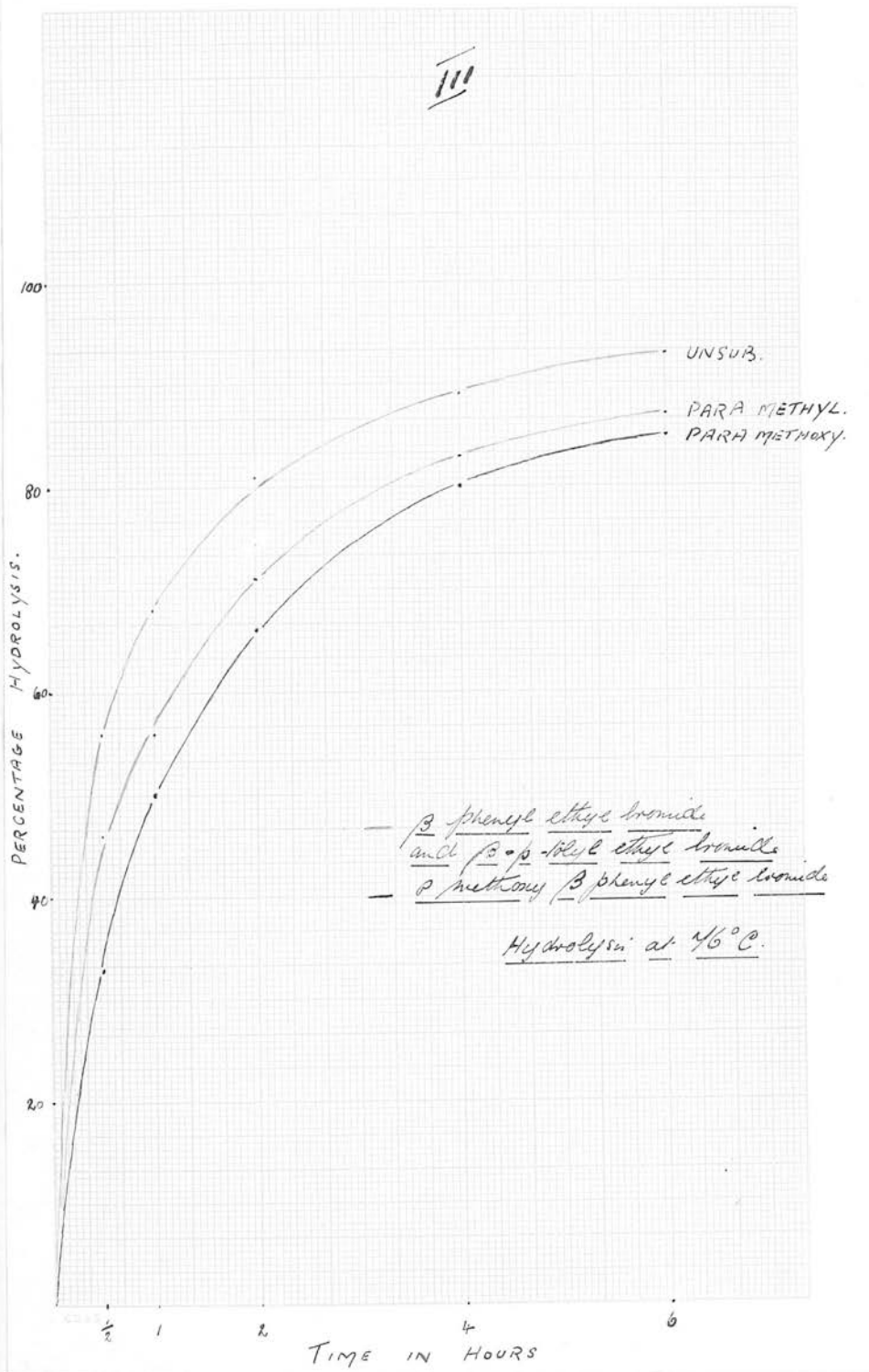
Graph I.


I.
100
80
60
40
20
PERCENTAGE HYDROLYSIS
UNSUB
META
PARA
ORTHO
½
1
2
4
6
TIME IN HOURS.
Phenyl ethyl bromide
and the Isomeric β Tolyl ethyl bromides
Hydrolysis at 46°C.

Graph II.


11
PARA.
ORTHO.
META.
UNSUB.
100
80
60
40
20
PERCENTAGE HYDROLYSIS
½
1
2
3
TIME IN HOURS.
Benzyl bromide
and w brom xylenes.
Hydrolysis at 60°C.

Graph III.


III
100
80
60
40
20
PERCENTAGE HYDROLYSIS.
UNSUB.
PARA METHYL.
PARA METHOXY.
β phenyl ethyl bromide
and β-p-tolyl ethyl bromide
p methoxy β phenyl ethyl bromide
Hydrolysis at 46°C.
½
1
2
4
6
TIME IN HOURS

Reduction.

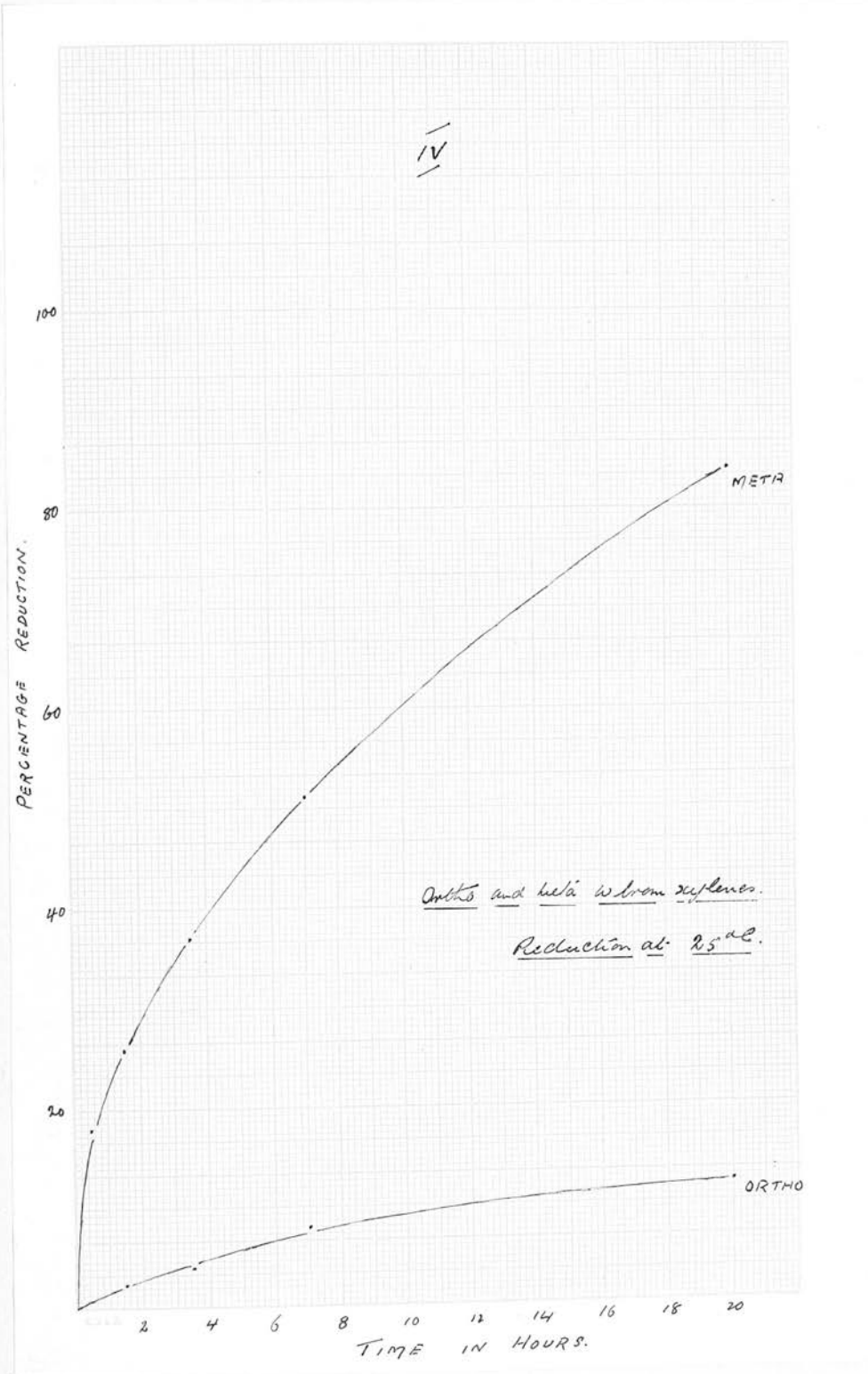
The order of reactivity of the Bromine atom of the $-CH_2CH_2Br$ group in the β tolyl ethyl bromides on reduction should, if there is any residuum of alternate effect, be ortho and para > meta. It was anticipated however from comparison with the w brom xylenes and the fact that hydrolysis of the β tolyl ethyl bromides required vigorous measures that reactivity of the Br atom towards HI would not be very apparent.

A strong reducing agent was used - constant boiling HI in glacial acetic acid at 100° C- and the reductions were carried on for four hours, but the maximum reduction as evidenced by the amount of iodine liberated was approximately 5%. No alternation in reactivity was observed.

For comparative purposes the reduction curves of the w brom xylenes are given in graph IV. These reductions were carried out at 25° with the same reducing agent.

The para isomer did not reduce under these conditions and iodine corresponding to 2% reduction was liberated from benzyl bromide.

Graph IV.


IV
100
80
60
40
20
PERCENTAGE REDUCTION.
META
ORTHO
Ortho and meta w. brom xylenes.
Reduction at 25° C.
2
4
6
8
10
12
14
16
18
20
TIME IN HOURS.

PREPARATIVE.

Three methods of preparation of the various substituted β phenyl ethyl bromides were investigated.

They are summarised in the following schemes:-

① $R\,C_6H_4CHO + CH_3NO_2 \xrightarrow{\text{alkali}} R\,C_6H_4CH = CH\,NO_2$

$R\,C_6H_4CH_2.CH:NOH \xleftarrow{\text{zinc dust}}$ $R\,C_6H_4CH = CH\,NO_2$ $\xrightarrow{\text{Na amalgam}}$ $R\,C_6H_4CH_2CH_2NH_2$

$R\,C_6H_4CH_2CH_2NH_2 \xrightarrow{HNO_2} R\,C_6H_4CH_2CH_2OH \xrightarrow{PBr_5} R\,C_6H_4CH_2CH_2Br$

② $R\,C_6H_4CHO \xrightarrow{CH_2(COOH)_2} R\,C_6H_4CH:CH.COOH$

$R\,C_6H_4CH_2CH_2COOH \xleftarrow{\text{Na amalgam}}$ $R\,C_6H_4CH:CH.COOH$ $\xrightarrow{SOCl_2\ \&\ NH_4OH}$ $R\,C_6H_4CH_2CH_2NH_2$

$R\,C_6H_4CH_2CH_2NH_2 \xrightarrow{HNO_2} R\,C_6H_4CH_2CH_2OH \xrightarrow{PBr_5} R\,C_6H_4CH_2CH_2Br$

③ $R\,C_6H_4\,Br \xrightarrow[\text{and } CH_2Cl\,CH_2OH]{\text{Mg compound}} R\,C_6H_4CH_2CH_2OH \xrightarrow{PBr_5} R\,C_6H_4CH_2CH_2Br$

As will be seen later the first method failed because of the poor yield of amine obtained.

The second method was more successful for the preparation of the amine but the action of HNO_2 in presence of HCl gave an alcohol contaminated with a chloride, and when H_2SO_4 was used a poor yield of impure alcohol was obtained.

The third method was successful in the preparation of the substituted β phenyl ethyl alcohols.

The final stage in the synthesis i.e. the bromination/

bromination of these substituted alcohols was successful in the methyl substituted compounds, but failed in the preparation of the methoxy substituted compounds.

I) This synthesis was attempted with meta methoxy benzaldehyde as the initial substance and this substance presented no difficulty in its preparation.

m met hoxy styrol. (Thiele, Annal. Zr. 325 7)

A solution of 28 grams of m. methoxy benzaldehyde and 13 grams of nitro methane in 40 c.c. of alcohol was vigorously stirred whilst 23 c.c. of 25% methyl alcoholic KOH were added slowly. This was followed by the addition of a solution of 4 grams NaOH in 20 c.c. of water and the mixture which became almost solid was stirred until a sample poured into water gave a clear solution. The whole was then added to a large quantity of ice water and when it was completely in solution it was decomposed with the calculated quantity of ice cold H_2SO_4. The solid m methoxy nitro styrol was filtered, well/washed with ice cold water and finally dried and recrystallised from alcohol. It crystallised in light yellow plates and had a melting point of 93°-94° C. This new styrol was analysed and it contained

7.99% N_2

$C_9H_9NO_3$ requires 7.82% N_2

The following modification of Rosenmunde's original reduction method (see Ber., 1909 42 4778) was the most satisfactory/

satisfactory method of converting this compound into the oxime of m methoxy phenyl acetaldehyde.

Oxime of m methoxy phenyl acetaldehyde.

m Methoxy ω nitro styrol (I3 grams) was mixed in a mortar with I3 grams of zinc dust and then added to a vigorously stirred mixture of 65 c.c. of alcohol and 26 c.c. of glacial acetic acid. The temperature was kept below 35° C. After I0 minutes a further 20 c.c. of alcohol were added and the temperature slowly allowed to fall to normal. The solid containing zinc oxide was then filtered off, washed with ether and the filtrate diluted with water. The ethereal layer which now separated was extracted with sodium carbonate to remove excess acetic acid and then three times with NaOH to extract the oxime. Sodium bicarbonate solution was added to the oxime solution and the precipitated oxime was filtered off, recrystallised first from ligroin and then from water from which it crystallised in white needles of melting point 92.5° - 93° C.

This new oxime was analysed and it contained

8.50% N_2

$C_9H_{II}NO_2$ requires 8.49% N_2

Attempts were now made to reduce the compound to m methoxy β phenyl ethyl amine but the yields of amine hydrochloride obtained (about 5% of that expected) were so poor that the method was abandoned.

2/

2) Substituted methoxy benzaldehyde.

The only compound which presented difficulty in its preparation was o methoxy benzaldehyde. A very successful method for its preparation was worked out:

O methoxy benzaldehyde.

There is no satisfactory method given in literature for the preparation of large quantities of o methoxy benzaldehyde from salicylaldehyde. The following method was found to be very satisfactory.

Salicylaldehyde (I molecule i.e. I22 grams) was vigorously stirred with about 40 c.c. of water in a flask fitted with a stopper carrying a stirrer, a condenser and two dropping funnels. Potassium hydroxide (I½ molecules i.e. 85 grams) was dissolved in I60 c.c. of water and dimethyl sulphate (I¼ molecules i.e. I57 grams) were placed in each of the dropping funnels and then allowed to flow into the salicylaldehyde alternately. The yellow colour of the potassium compound of salicyl aldehyde was an indicatdon of the course of the reaction and the addition was so regulated that the colour was first produced by KOH and then dissipated by $(CH_3)_2SO_4$. In this way excess of KOH and $(CH_3)_2SO_4$ was avoided and no cannizzaro reaction could take place. The addition took about one hour to complete. The whole was allowed to cool and the oil produced extracted with KOH solution to remove unchanged salicylaldehyde. The o methoxy benzaldehyde was extracted with ether, dried and/

and ether distilled off. The residue distilled at 235° - 237° C and the yield obtained was 99 grams i.e. 72% of the theoretical.

Isomeric methoxy cinnamic acids.

(Haworth, Perkin and Rankin J. 1924 125 1694)

$$C_6H_4OCH_3CHO + CH_2(COOH)_2 \longrightarrow C_6H_4OCH_3CH{:}CH.COOH + CO_2 + H_2O$$

The isomeric methoxy benzaldehyde reacted with malonic acid in pyridine solution with evolution of CO_2 to form the isomeric methoxy cinnamic acids. Pyperidine was used as a catalyst in the reaction.

The ortho and para acids were readily separated by pouring the reaction mixture into excess water but the meta acid was appreciably soluble and a smaller volume of water was required. The products were re-crystallised from acetic acid. The melting points were as follows:-

o.acid = 180° - 182° C.

m.acid = 120° - 121° C.

p.acid = 174° - 175° C.

Cinnamic acid and its substituted derivatives exist in cis and trans forms. The possibility that the meta acid was either "cis"or "trans" or a mixture of both isomers was investigated by preparing m.hydroxycinnamic acid from m.hydroxy benzaldehyde and malonic acid as above, and methylating this compound by allowing

it/

it to stand with methyl iodide in methyl alcoholic KOH solution. Any unchanged hydroxy acid was separated from methylated acid by means of diazotised sulphanilic acid with which the hydroxy acid gives a soluble deep red dye.

The methoxy acid was recrystallised from dilute acetic acid and had a melting point of II9° C. The acid prepared above from m methoxy benzaldehyde had a melting point of I20° - I2I° C thus the meta acid was not a mixture of isomers.

Isomeric methoxy hydrocinnamic Acids.

(Perkin & Robinson J. I907 93 I079)

The methoxy cinnamic acid in alkaline solution was vigorously stirred and the requisite quantity of 3% sodium amalgam added in small quantities. Concentrated HCl was simultaneously added drop by drop in order that the concentration of alkali should not become too great and cause the loss of CO_2 from the carboxyl group. The solution on cooling was acidified and the methoxy hydrocinnamic acid was precipitated.

The most successful yield was obtained when the temperature of the reaction mixture was raised quickly by adding the sodium amalgam quickly to the warm solution.

Isomeric methoxy β phenyl propionamides.

Two/

Two methods were used.

I) The amide was prepared directly from the substituted hydrocinnamic acid by passing a stream of dry ammonia gas into the acid maintained at 220° - 230° C. for two hours. The temperature is a very important factor and any elevation of the temperature resulted in tarring. The yield was poor.

2) The following method was much more successful.

The dry methoxy hydrocinnamic acid was dissolved in dry chloroform and I - I½ molecules of thionyl chloride added. The reaction mixture guarded by a calcium chloride tube was allowed to stand overnight and then poured into ammonia (D 0.880) which contained a small quantity of NaOH. The whole was kept cool in ice water. The chloroform was rapidly distilled off and with it a proportion of the ammonia. (This operation was done in the open air). The residue was filtered hot and the amide separated from the filtrate. The quantities used were :-

50 grams methoxy hydrocinnamic acid

170 c.c. dry chloroform

37 c.c. thionyl chloride

600 c.c. ammonia (D 0.880) containing

20 grams NaOH in the minimum quantity of water.

The ortho and para amides were found to separate partially from the chloroform-ammonia solution before distillation. The yields obtained were:-

o amide/

o amide 85%

m & p amides 80%

No melting points were taken.

Isomeric Anisyl ethyl amines.

(Buck and Perkin J. 1924 125 1679)

Sodium hypochlorite was prepared by passing chlorine prepared from $KMnO_4$ and HCl into ice cold NaOH solution. The amide was added to this hypochlorite solution and the temperature gradually raised to 70° - 75° C and maintained there for one hour. The reaction mixture was allowed to cool for two hours and the amine extracted with benzene, dried and precipitated as the hydrochloride.

At this stage in the synthesis the amines were purified.

Purification of the Amines.

Each amine hydrochloride was dissolved in water and the solution extracted with ether. The aqueous solution after evaporating off dissolved ether was made alkaline with NaOH. A red liquid was separated off, washed with water, dried and distilled in vacuo.

The boiling points were as follows:-

β phenyl ethyl amine	87° - 88°/18 m.m.
o anisyl ethyl amine	127° - 128°/21 m.m.
m " " "	126° - 127°/14 m.m.
p " " "	131° - 132°/18 m'm.

phenyl/

β phenyl ethyl amine had been prepared coincident with the substituted β phenyl ethyl amines by the same methods and it was now used to determine the conditions for the preparation of the alcohols.

β phenyl ethyl alcohol.

β phenyl ethyl amine hydrochloride was prepared by passing hydrogen chloride into a concentrated benzene solution of the amine. The resulting solid hydrochloride was filtered and dried.

It was then dissolved in the minimum quantity of water, one molecule of HCl added followed by I½ molecules of $NaNO_2$ dissolved in water the solution being mechanically stirred and cooled below 0° C. during the operation.

After two hours stirring the reaction was completed by heating for 30 minutes on the water bath when a red oil separated out. When this liquid was distilled in vacuo two fractions were obtained-

Fraction A 82° - 87° /2I m.m.

and Fraction B 95° -105° / 2I m.m.

A contained hydolysable chlorine and a trace of nitrogen B contained a trace of hydrolysable chlorine and no nitrogen.

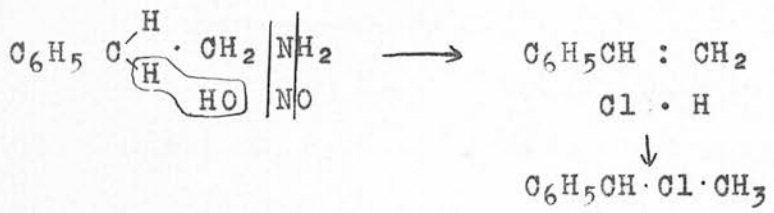
The lower boiling fraction A was proved to be β phenyl ethyl chloride. The higher boiling fraction B was β phenyl ethyl alcohol contaminated with β phenyl ethyl chloride/

chloride.

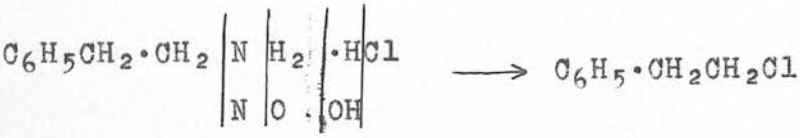
Note:

The chloro compound must be either $C_6H_5CHCl.CH_3$ or $C_6H_5CH_2CH_2Cl$.

The first would be formed if the reaction taking place was as follows:-



The second compound would be formed if the following reaction took place -



The compound was proved to be $C_6H_5CH_2CH_2Cl$ by nitrating in the para position pure β phenyl ethyl chloride and also nitrating the lower boiling fraction A . The resulting solids were recrystallised and a mixed melting point taken. The methods and results are given below.

β phenyl ethyl chloride.

(Barger J. 1909 95 2193).

β phenyl ethyl alcohol (commercial product) was added drop by drop to a mixture of PCl_5 and chloroform. The reaction was completed by warming on the water bath for two hours. After the removal of $CHCl_3$ and $POCl_3$ the residue/

residue was fractionated in vacuo when β phenyl ethyl chloride distilled at 90° - 95° C/ 22 m.m. the bulk coming over at 92° / 22 m.m.

nitro β

P nitro β phenyl ethyl chloride.

(Barger loc.cit.)

It was prepared by nitrating β phenyl ethel chloride at -I5° C with fuming HNO_3 (D I.5). After pouring on to ice and extracting, the product was distilled and two fractions collected i.e. I65° - I75° /I8 m.m.

and I75° - I79° /I8 m.m.

The higher fraction crystallised out on cooling. It was recrystallised twice from 40° - 60° petrol ether and gave a melting point of 47° - 48° C. (Barger 49° C.) (Braun (Ber. 45 I276) repeated Barger's work and gave the melting point as 48° C. He also stated that no ortho derivative was formed on nitration at low temperature).

The lower boiling fraction from the alcohol prepared from β phenyl ethyl amine was nitrated as before and the resulting solid on recrystallising twice from 40° - 60° petrol ether, gave a melting point of 47° C.

It did not depress the melting point of the nitro compound prepared from the pure chloride. Microscopic examination revealed no difference in the crystalline form which was plates.

Thus the lower boiling fraction was proved to be/

be almost completely β phenyl ethyl chloride.

Isomeric methoxy β phenyl ethyl alcohols.

In view of the above fact HCl was replaced by H_2SO_4 in preparing HNO_2.

Dilute H_2SO_4 was added to the amine and the amine sulphate was redissolved in excess of dilute acid. After carrying out the reaction as before the product was steam distilled, the distillate extracted, dried and distilled in vacuo.

In each case a very poor yield of the methoxy β phenyl ethyl alclhol was obtained distilling over a range of 10° C and containing traces of unchanged amine.

Attempts to brominate these impure alcohols were unsuccessful and the synthesis was abandoned.

3) Preparation of the ismoeric methoxy β phenyl ethyl alcohols by the third synthesis.

The initial compounds are the isomeric brom anisoles which were prepared as follows:-

p brom anisole.

p brom phenol (Organic Synthesis I 39).

Phenol in CS_2 solution was brominated below 5° C by the slow addition of a solution of bromine in CS_2. After the removal of CS_2 the resulting liquid was fractionated in vacuo when it distilled completely at 115° - 122°/16 m.m. with the bulk distilling at 118° - 119°/16 m.m. The yield/

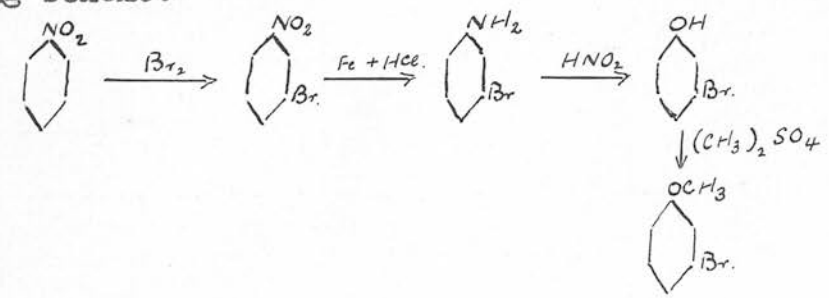
yield was 960 grams from 750 grams of phenol. M.P. 64° C.

p brom anisole.

Quantities of 100 grams each of p brom phenol were methylated by the addition of a solution of 18 grams NaOH in 150 c.c. of water and 48 grams of dimethyl sulphate. This mixture was shaken under a reflux condenser for 15 minutes, 20 grams of NaOH were added and the reaction mixture was boiled for three hours. Ten c.c. of dimethyl sulphate were now added and boiling continued for another four hours. An oil separated, which was washed several times with dilute NaOH, to remove traces of phenol, and then with water, dried and distilled using a four bulb fractionating column. p brom anisole distilled at 217° - 221° C. The yield was 270 grams from 300 grams of p brom phenol.

m brom anisole.

This compound was prepared according to the following scheme:-



The four stages are described as follows:-

1.) m brom nitro benzene.

Wheeler and McFarlane (Amer. Chem. J. 1891 19 366)./

366).

Nitrobenzene was heated in a flask to I20° C in presence of a halogen carrier, iron wire, and bromine slowly added. After the mixture had been heated for two hours at I20° C it was steam distilled and the first fraction which contained excess bromine was discarded. The solid m brom nitrobenzene was filtered, dried and recrystallised from 96% alcohol.

The quantities used were four times these stated in the literature i.e.

I20 grams nitrobenzene

I2 grams iron wire

240 grams bromine.

The yield obtained was I40 grams.

2) m brom aniline.

(R.W.West J. I925 I27 494)

One gram molecule of m brom nitro benzene was heated to boiling with 500 c.c. 96% alcohol containing I0 c.c. concentrated HCl. I70 grams of fine iron filings were introduced in four portions with an interval between each addition. The mixture was heated for two hours, made alkaline and steam distilled. The product after extraction with ether, drying and removal of ether, was distilled at 250° - 260° C but slight decomposition took place and distillation in vacuo was used in subsequent preparations.

Note: Unchanged m brom nitro benzene was removed by forming/

forming the aniline hydrochloride which was filtered and washed and dissolved in hot water. A slight quantity of unchanged m brom nitro benzene separated out.

Ultimately the reduction was so successful that no unchanged m brom nitro benzene was obtained.

3) m brom phenol.

It was formerly very difficult to obtain a good yield of m brom phenol by the diazotisation of m brom aniline. [Diels and Bunzl (Ber.1905 38 1496) give a method with only a 22% yield].

However a method of carrying out the diazotisation was suggested by Dr H. H. Hodgson (cf.Brit.Pat. 200714) and proved to be very successful.

m brom aniline sulphate was formed from 50 grams m brom aniline and dissolved completely in hot dilute H_2SO_4 of the requisite quantity to form a thin paste on cooling. This paste was cooled to 0° C, mechanically stirred and 30 grams solid $NaNO_2$ added in small quantities. About four hours were occupied in this addition. Ten grams urea were then added to destroy excess HNO_2 and the resulting diazotised solution added to 200 c.c. H_2SO_4 (I part concentrated acid : I part water) through which a brisk current of steam was passed. M brom phenol readily distilled in steam and, contrary to literature is appreciably soluble in water. After extraction and drying, it was fractionated in vacuo/

vacuo. It distilled at about 120°/13-14 m.m.

The yield varied from 80% - 90% of the theoretical.

4) m brom anisole.

It was prepared by methylating m brom phenol by the same method as was used above in the methylation of p brom phenol.

The boiling point was 214°/729 m.m. and the whole distilled at 211.5 - 214.5 /729 m.m.

There was no trace of phenol present.

The yield from 210 grams m brom phenol was 160 grams.

o brom anisole.

It was prepared by the methylation of o brom phenol. This appears to be the first time this method has been tried for preparing o brom anisole.

The method of methylation was the same as that used in preparing the meta and para isomers.

The yield obtained was 80% of the theoretical The literature on the subject gives the following boiling points for this compound:-

Walloch, Heusler (A 243 237) = 221°-223°

Michaelis, Geisler(B.27 256) = 210°

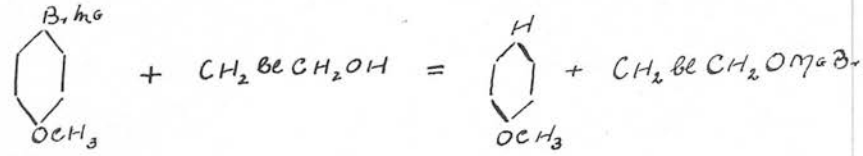
Grande (G. 27 II 67) = 217.5°- 218.°

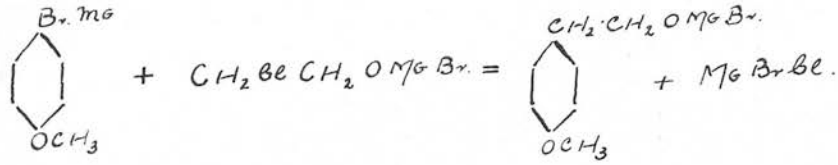
An accurate determination of the boiling point was made and found to be 220°/743.5 mms.

Preparation/

Preparation of the Isomeric methoxy β phenyl ethyl alcohols.

V. Grignard (Comptes Rend. 1905 I4 I 44) obtained p methoxy β phenyl ethyl alcohol by preparing the magnesium compound of p brom anisole and allowing it to react with ethylene chrorhydrin according to the equations –





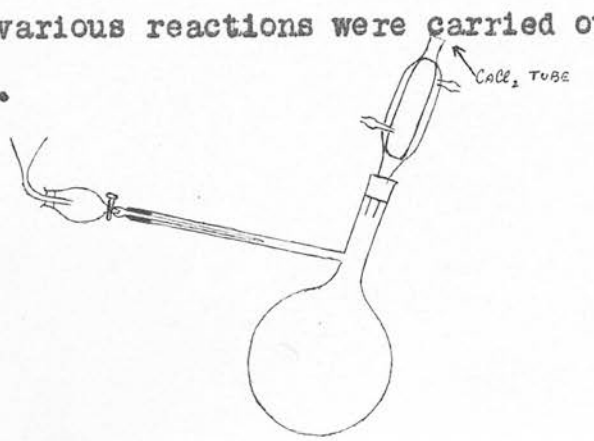
This reaction, though requiring extreme care, was successfully used for the preparation of all the isomeric methoxy β phenyl ethyl alcohols.

The general method used was as follows:-
I.5 molecules brom anisole and I.5 atoms magnesium in 250 c.c. dry ether were allowed to react in an apparatus which is detailed below. When the reaction was complete, 0.5 molecule of ethylene chlorhydrin in an equal volume of dry ether was slowly added, shaking constantly. The reaction was vigorous and it was carried to completion during the slow distillation of the ether. At the end of this distillation the residue frothed up. This however/

however made the resulting solid porous in nature and facilitated the removal of impurities, The residue which was dark brwon was heated at about 180°/14 m.m. for two hours to remove impurities. An optimum temperatyre had to be found for each compound as tarring readily took place at this stage. The impurities included anisole and the isomeric dianisoles.
The magnesium alcoholate which did not distil at this temperature was ground up with ice and left for 30 minutes. The necessary quantity of H_2SO_4 in ice water to dissolve the magnesium was now added drop by drop, stirring continuously. After leaving for three hours the product which in ortho and para isomers coagulated into semi solid masses, was extracted with ether, dried over anhydrous Na_2SO_4, and the ether removed. The residue was heated on a water bath for 10 minutes with 25 c.c. of 10% alcoholic KOH to remove traces of halogen Excess water was added and the whole extracted and dried as before. The red coloured liquid residue was distilled in vacuo using a Widmer column (Helv.Chim. Acta 1924 7 59) in the Claisen flask.

Note on the apparatus used.

The following diagram indicates a method in which the various reactions were carried out in the same flask.



A two litre distilling flask with a wide side tube to allow the introduction of a dropping funnel was used. The magnesium, ether and the brom anisole were allowed to react in the flask and ethylene chlorhydrin was then introduced through the dropping funnel. The dropping funnel was removed and the double surface condenser replaced by a rubber stopper. The ether was then distilled off in the ordinary way and a Collie flask was attached to the side tube to collect the impurities removed under reduced pressure. The powdery residue was easily removed from the flask.

Below is given the results of the preparation of the isomeric methoxy β phenyl ethyl alcohols.

O methoxy β phenyl ethyl alcohol.

The optimum temperature for the removal of impurities was 150° - 160°/15 m.m. This temperature did not remove all the impurities but it was found expedient to remove any higher boiling impurity in the fractionation of the final product and thus avoid possibility of tarring.

The boiling point was 130°-131.5°/13 m.m. At -5°C the colourless liquid was very viscous. On analysis the compound contained

71.8% carbon

7.77% Hydrogen

$C_9H_{12}O_2$ requires 71.1% carbon
7.89% Hydrogen

m methoxy/

m Methoxy β phenyl ethyl alcohol.

The optimum temperature in the removal of impurities was 160°-170° / 15 m.m. The product on the addition of H_2SO_4 did not coagulate into lumps as in the ortho and para isomers but remained as an oil. The boiling point was 135° - 138°/12 m.m. The colourless liquid did not solidify after long standing at -5° C.

On analysis the compound contained

71.11% Carbon

7.59% Hydrogen

$C_9H_{12}O_2$ requires 71.1% Carbon

7.89% Hydrogen.

p methoxy β phenyl ethyl alcohol.

The optimum temperature on the removal of impurities was 160°/12-15 m.m.
The boiling point was 136° - 140°/11 m.m. and the melting point of the white crystalline solid obtained on cooling below 0° C was 24° C.

(Grignard (loc.cit.) B.P. = 143° - 144°/13 m.m.

M.P. = 24° C.)

In each case above the yields obtained were approximately 25% of the expected.

Preparation of the Isomeric β phenyl ethyl bromides.

After preliminary experiments the following conditions were used for the bromination of the para alcohol/

alcohol.

Phosphorus pentabromide (I½ molecules i.e. 35 grams) and 50 c.c. dry benzene were placed in a small flask to which an air condenser was attached and IO grams of p methoxy β phenyl ethyl alcohol were added a few drops at a time. The contents of the flask were vigorously shaken and kept cool in ice water. The operation occupied 30 minutes. The mixture was then transferred to a Claisen flask with a wide air leak and air, dried by passage through $CaCl_2$ and P_2O_5 towers was aspirated through the solution in order to remove the hydrogen bromide as soon as it was formed. This operation occupied 3 - 4 hours. During this time the PBr_5 slowly disappeared. The resulting red solution was heated on a water bath at 50°C for 30 minutes cooled and poured on to ice in order to decompose the $POBr_3$ which was formed in the reaction. The benzene solution of the bromide was then separated and washed several times with water to remove all traces of $POBr_3$ and dried over Na_2SO_4 and the benzene distilled in vacuo. The residue was again washed with water and extracted and dried as before. The final fractionation using a Widmer Column yielded an oil of boiling point I30-I3I°/ II m.m. Three grams of a colourless liquid were obtained.

The compound on analysis contained

35.0% of hydrolysable bromine

$C_9H_{11}OBr$ requires 37.2% hydrolysable Bromine.

Note An estimation of the percentage of hydrolysable bromine was obtained by heating a weighed quantity (0.15 grams) of the substance with 10 c.c. of 10% alcoholic KOH for 30 minutes, cooling and acidifying with 5 c.c. of concentrated HNO_3. Ten c.c. of N/10 $AgNO_3$ were added and the excess $AgNO_3$ was back titrated with N/10 NH_4CNS using ferric indicator.

M methoxy β phenyl ethyl bromide.

The same method of bromination was used. A poor yield of a yellow liquid was obtained and it was distilled at 135° - 150°/12 m.m. Above 150°/12 m.m. decomposition took place and fumes of HBr were observed. The product on analysis contained

30.6% of hydrolysable bromine

$C_9H_{11}OBr$ requires 37.2% hydrolysable Br.

The result of analysis seemed to indicate incomplete bromination and so a further 10 grams of meta alcohol was brominated, the conditions being modified so that the solution after heating to 50°C and left in the cold for several hours was again shaken up with PBr_5 (½ molecule i.e. 14 grams) and decanted on to ice as before. The product was fractionated in vacuo and it distilled at 163° - 165°/13 m.m.

On analysis it contained 27.2% hydrolysable bromine.

$C_9H_{11}OBr$ requires 37.2% hydrolysable Bromine.

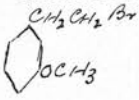
To/

To explain this result three possibilities were considered.

I) Demethylation by free hydrogen bromide may have taken place. In the above method an attempt was made to prevent this by removing the HBr from the system at once.

2) Nuclear bromination may have taken place possibly subsequent to demethylation.

3) A compound of the nature $OCH_3C_6H_4CH_2.CH_2OPBr_2$ may have been formed (cf.Boyd J. 1926 2323).
The abnormal elevation of the boiling point of the bromide in comparison with the alcohol also indicated nuclear bromination. In order to examine the possibilities several analyses were performed.

An estimation of the percentage of methoxyl (OCH_3) group by Zeisel's method was carried out. The compound contained 2.33% OCH_3  requires I4.4% OCH_3.

An estimation of the total bromine by Carius' method was carried out. The compound contained 53.8% bromine

$OCH_3C_6H_3Br\_CH_2CH_2Br$ requires 54.4% Bromine

$OCH_3C_6H_4CH_2CH_2Br$ requires 37.2% Bromine

Tests for the detection of phosphorus failed. It was thus inferred that demethylation and nuclear bromination had taken place.

PBr_5/

PBr_5 was the only suitable brominating agent. The choice was restricted since gaseous HBr caused demethylation and had no effect on the alcohol and compounds of the nature R $C_6H_4CH_2CH_2OPBr_2$ were the probable result of the use of PBr_3 (see Boyd and Smith J.1926 I28 2326) A solution of hydrogen bromide in glacial acetic acid and constant boiling HBr solution both gave negative results.

Finally 10 grams m methoxy β phenyl ethyl alcohol were brominated at room temperature. 35 grams PBr_5 and 50 c.c. dry benzene were placed in a Claisen flask and 10 grams of the alcohol slowly added. As before dry air was aspirated through for several hours. The product was worked up as before without heating to 50° C and after washing with water and distilling off the ether and benzene in vacuo the residue was distilled under diminished pressure.

No definite fraction was observed. The boiling point was 132° - 150° /12 m.m. Slight decomposition took place above 150° /12 m.m. A trace of a white solid was observed on the neck of the Claisen flask.

The product contained 32.7% of hydrolysable Br. $OCH_3C_6H_4CH_2CH_2Br$ requires 37.2% hydrolysable Br.

It contained 40% of total bromine. $OCH_3C_6H_4CH_2CH_2Br$ requires 37.2% total Br.

It also contained 12.7% methoxyl group

OCH_3/

$OCH_3C_6H_4CH_2CH_2Br$ requires 14.4% (OCH_3)

Therefore slight nuclear bromination and demethylation again took place. It was thus found impossible to prepare m methoxy β phenyl ethyl bromide in the pure state.

O methoxy β phenyl ethyl bromide.

The same method and quantities were used as in the final preparation of the meta bromide above. Distillation in vacuo began at 130°/12 m.m. and slowly rose to 160°/12 m.m. when a definite fraction was observed at 160°-165°/12 m.m. which was collected separately. It solidified to a white crystalline solid (3 grams) which was crystallised from 96% alcohol in white needles and melted at 53° C.

After repeated recrystallisation the melting point remained sharp at 55° C.

This compound on analysis contained

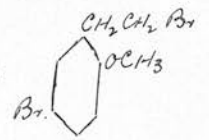
36.38% Carbon
3.51% Hydrogen
54.4% Total Bromine

This analysis corresponds with a compound of the formula $OCH_3C_6H_3Br\ CH_2CH_2Br$ which requires

36.7% Carbon
3.4% Hydrogen
53.7% Total Bromine

The percentage of hydrolysable bromine obtained also agreed with a compound of this composition (i.e. 27.2%)

O cresol brominates in the 5 position so the probable constitution of this compound is



Preparation of the isomeric β tolyl ethyl bromides.

p brom toluene

(Organic Synthesis 5 21)

P toluidine was converted to p brom toluene by the usual Sandmeyer reaction as follows:

$$CH_3C_6H_4NH_2 + HNO_2 + H_2SO_4 = CH_3C_6H_4N_2SO_4H + 2H_2O$$

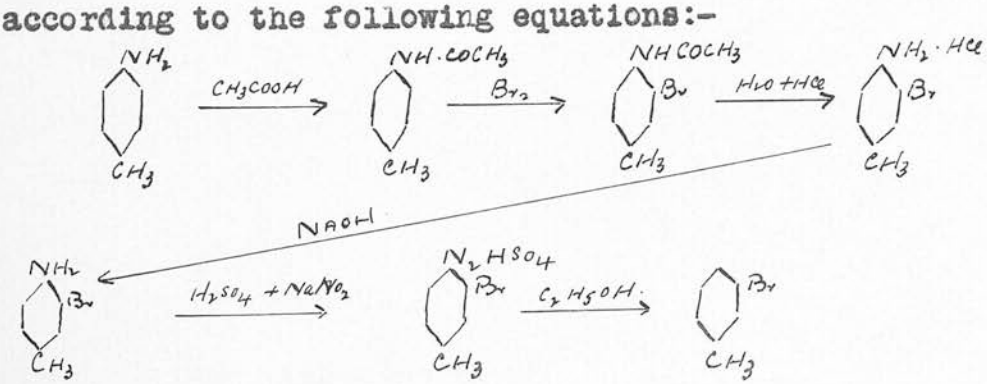
$$CH_3C_6H_4N_2SO_4H + HBr\ (+CuBr) = CH_3C_6H_4Br + N_2 + H_2SO_4$$

The Sandmeyer reagent, HBr - CuBr solution, was first prepared and the diazonium solution was added slowly to it. A current of steam was simultaneously passed through the heated solution. The p brom toluene resulting from this steam distillation was extracted, purified and distilled at 179° - 183° C. The yield was 100 -110 grams.

m brom toluene.

The method used above in the preparation of the para isomer was tried but the yield was poor. The diazonium compound was less stable than the corresponding para compound.

However a method (Organic Synthesis 6 8 & 16) was used successfully in which p toluidine after acetylation was brominated and subsequently diazotised according to the following equations:-



It was found advantageous in the separation of the amine hydrochloride to leave the solution for several hours. Also in extracting the impurities with concentrated H_2SO_4 only a small quantity of acid was used in each extraction since otherwise it was difficult to observe two layers.

After fractionation of the product the boiling point was I82° - I84° C. The yield was 90 grams from 2I4 grams of p toltdine.

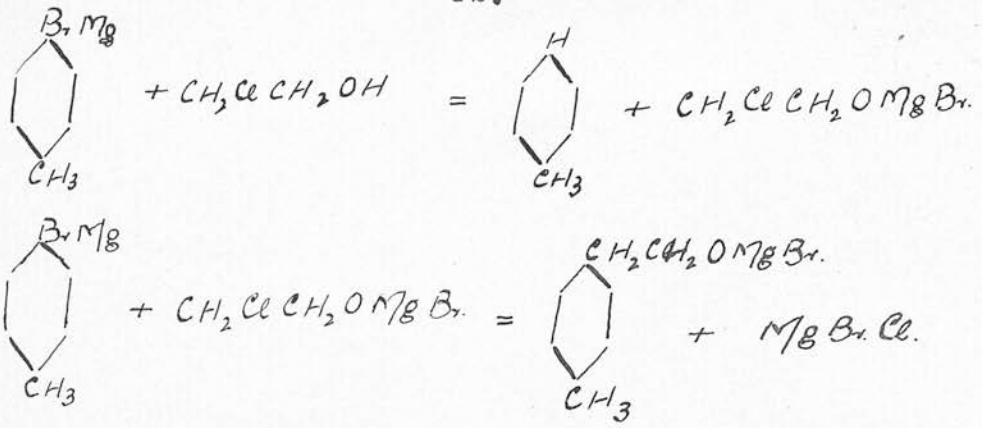
O brom toluene.

The method adopted was the one used in the preparation of p brom toluene. The instability of the diazonium compound resulted in a large decrease in yield which was only 25% of the theoretical.

The boiling point was I79° - I82° C.

Several methods were tried including a method by Acree (Ber.,I904 37 994) in which o toluidine was diazotised in HBr solution but there was only a slight improvement in yield and the above method was the most convenient.

The method used in the preparation of the isomeric β tolyl ethyl alcohols was the same as that described under the preparation of the isomeric methoxy β phenyl ethel alcohols. (Grignard Comptes Rend. I905 I4I 44)



The quantities used were as follows:-

64 grams brom toluene

9 grams magnesium

250 c.c. dry ether

10 grams ethylene chlorhydrin.

and the general procedure was the same.

Any modifications are detailed as follows:-

β p tolyl ethyl alcohol.

In removing impurities by heating in vacuo it was found that the optimum temperature was much higher than the methoxy substituted compounds i.e. 180° - 200°/14 m.m. The removal of pp' ditolyl presented difficulties. After a preliminary distillation of the final product it was cooled below 0° C. and separated from the white solid pp' ditolyl (M.P.=121° C, B.P.=295° C) by filtration through glass wool. When redistilled it had a boiling point of 116.5° - 118°/14 m.m.

[Grignard (Comptes Rend. 1905 141 44) B.P. 115° - 116°/13 m.m.]

β m tolyl ethyl alcohol.

There/

There was no modification of the method. The final fractionation was II4° - II7° /I3 m.m.
[Braun Grabowski & Kirschbaum (Ber. I9I3 46 I266)
I23° - I25° /I8 m.m.]

β o tolyl ethyl alcohol.

In this case the Grignard reaction was unsuccessful until traces of phenol and free halogen which were detected in the o brom toluene, were removed by washing with alkali, dilute H_2SO_4 and Na_2CO_3 solution After which the purified brom ~~e~~ toluene was dried and redistilled. The reaction was then successful. The boiling point of β o tolyl ethyl alcohol was II5° - II6° / I3 m.m. [Grignard (loc.cit.) II9° - I20° /I4 m.m.]

Preparation of the Isomeric β tolyl ethyl bromides from the corresponding alcohols by PBr_5.

The method of bromination was the same in each case. A detailed description is given of the procedure in preparing β m tolyl ethyl bromide.

Fifteen grams of meta alcohol were mixed with 50 c.c. dry benzene in a flask carrying an air condenser and I¼ molecules PBr_5 were added slowly. The flask was continually shaken and kept cool in ice water. The reaction was vigorous and hydrogen bromide was continually evolved. After the reaction had modified the whole/

whole was heated in a water bath to 50°C for one hour when there was no further evolution of HBr. The unchanged PBr_5 and $POBr_3$ were decomposed by pouring on to ice, which was extracted with ether. The ethereal layer was dried over Na_2SO_4, and after the removal of ether the residue was distilled twice in vacuo using a Widmer column.

In order to obviate any possibility of undecomposed $POBr_3$ being present the yield was washed subsequently with water, dried and redistilled.

Compounds.	Percentage hydrolysable Br.	Boiling Points.
β p tolyl ethyl bromide	% found 40.3% $C_9H_{11}Br$ requires 40.2%	99°-100° /10 m.m.
β m tolyl ethyl bromide	% found 39.8% $C_9H_{11}Br$ requires 40.2%	101°-103° /11 m.m.
β o tolyl ethyl bromide	% found 39.4% $C_9H_{11}Br$ requires 40.2%	103.5°-105° / 11 m.m.

In order to investigate if any nuclear bromination had taken place a total bromine estimation by the method of Carius was carried out on β m tolyl ethyl bromide.

The compound was found to contain 40.0% total bromine and $C_9H_{11}Br$ requires 40.2% total bromine.

Thus no nuclear bromination had taken place.

Preparation of β phenyl ethyl bromide.

β phenyl ethyl alcohol was brominated by PBr_5 using/

using the same method as was detailed for the preparation of the methyl substituted derivatives.

The boiling point was 89° - 89.5°/12 m.m. and the yield was 60% of the theoretical. The compound was analysed and contained 42.4% of hydrolysable bromine. C_8H_9Br requires 43.2% hydrolysable bromine.

A second very successful method (suggested to us by Professor Lapworth) was also used.

Twenty grams β phenyl ethyl alcohol and 50 c.c. constant boiling hydrobromic acid solution (B.P. = 123°/730 m.m.) were refluxed for four hours. The two layers were separated and the bromide layer was washed with water until no free halogen was detected, dried and distilled in vacuo.

The boiling point was 89° - 89.5°/12 m.m. The compound on analysis contained 42.4% hydrolysable bromine.

C_8H_9Br requires 43.2% hydrolysable bromine.

In the bromination of β phenyl ethyl alcohol and its substituted derivatives there is the possibility of the formation of isomers e.g.

$C_6H_5CH_2CH_2Br$ and $C_6H_5CHBr\,CH_3$

In order to investigate this possibility β phenyl ethyl bromide was prepared by using two different brominating agents HBr solution and PBr_5. The product obtained/

obtained in each case had the same boiling point and the same percentage of hydrolysable bromine. If either of the bromides obtained were a mixture of isomers or one was an isomer of the other then it was anticipated that the action of hydrolysing agents would show a variation in the rate of hydrolysis.

A hydrolysis of each sample was carried out as follows:-

0.099 gram of β phenyl ethyl bromide (PBr_5 method) and 0.IOI gram of β phenyl ethyl bromide(HBr method) were hydrolysed by a solution of alcoholic NaOH prepared by adding 5 c.c. of N/IO NaOH to the standard flask and making the volume up to 25 c.c. with absolute alcohol. The flasks were heated to 76° for two hours and the unused alkali titrated with N/IO HCl in the usual way.

β phenyl ethyl bromide (PBr_5 method) was hydrolysed to the extent of 41% and β phenyl ethyl bromide (HBr method) to the extent of 40%.

The possibility of the presence of isomers is thus remote.

In order to substantiate this result in the β tolyl ethyl bromide series the preparation of β-p-tolyl ethyl bromide with constant boiling HBr solution was attempted but was unsuccessful.

EXPERIMENTAL.

Rate of Hydrolysis.

A series of preliminary experiments were performed in order to determine the conditions under which the rate of hydrolysis could be compared most satisfactorily.

Firstly the behaviour of the bromides towards aqueous alcohol was investigated. A quantity of β p. tolyl ethyl bromide (.098 gram) was weighed into a 25 c.c. standard flask. 20 c.c. of absolute alcohol added and the volume made up to 25 c.c. with water. The flask was heated for four hours at 61° C by suspending it in a flask fitted with a double surface condenser and containing boiling chloroform. The vapour of the chloroform kept the contents of the flask at the required temperature thus acting as a simple thermostat. The contents of the flask were washed into a conical flask containing water and titrated with N/20 NH_4OH. The titration was 0.2 c.c. and thus hydrolysis in aqueous alcohol at 61° is negligible. Also free halogen impurity was absent.

A similar experiment was carried out, the hydrolysing agent being alcoholic NaOH. In a 25 c.c. standard flask containing 0.073 gram of β p.tolyl ethyl bromide 5 c.c. N/20 NaOH were placed and the volume made/

made up to 25 c.c. with absolute alcohol. The whole was heated at 61° C for four hours and titrated with N/20 HCl. The titration was 4.05 c.c. On comparison with a blank experiment which required 6.70 c.c. the percentage hydrolysis was 45%. The same concentration of alkali at 76 C (i.e. the vapour of boiling CCl_4) hydrolysed 71% and in the case of β m tolyl ethyl bromide hydrolysed 74%.

It was thus concluded that hydrolysis did not take place readily and that appreciable differences in the rate of hydrolysis would not be observed. In order to magnify these differences as much as possible the first series of hydrolysis experiments were made at 25° C. over a period of 8 days.

Approximately 0.55 gram of β phenyl ethyl bromide and the isomeric β tolyl ethyl bromides were weighed into 250 c.c. standard flasks. Thirty c.c. of N/10 KOH were added and the volume was made up to 250 c.c. with absolute alcohol. The flasks were placed in a 25° thermostat and 25 c.c. of the solution was titrated each morning with N/20 HCl.

The results are summarised in the following table in which w, represents the weight in grams used, t, the time in days from the commencement of the experiment and x the percentage hydrolysed.

Table/

TABLE I.

	unsub.	o isomer	m isomer	p isomer
w	0.559	0.594	0.578	0.542
t	x	x	x	x
I	I0.9	II	II.3	7.3
2	24.2	I9.3	20.0	I7.3
3	32.6	24.I	27.7	2I.3
4	37.5	30.7	34.7	26.7
5	43.I	33.0	40.7	34.0
6	47 4	39.0	44.4	38.4
7	50.9	44.2	48.6	44.0
8	5I.7	45.2	49.2	45.I

A second series of hydrolysis were carried out at 76°C. It was calculated that for a definite concentration of alcoholic NaOH the equivalent quantities of β phenyl ethyl bromide and the isomeric β tolyl ethyl bromides were 0.45 gram and 0.50 gram respectively.

The following method was adopted as the most suitable.

Hydrolysis of β phenyl ethyl bromide and the isomeric β tolyl ethyl bromides

In a I00 c.c. standard flask containing the requisite weight of the compound to be hydrolysed there were placed 75 c.c. of absolute alcohol and 25 c.c. of N/I0 NaOH and the volume made up with absolute alcohol to about I03 c.c. The contents of the flask were thoroughly mixed and 20 c.c. of the solution pipetted into five standard 25 c.c. flasks and each flask heated in the vapour of CCl_4 (i.e.76°C) for a specified time, the/

the periods being ½ hour, I, 2, 4 and 6 hours.

The whole operation of placing the solution in the flask was completed within IO minutes and no appreciable hydrolysis would result during this short period in the cold. After each hydrolysis the contents of the flask were poured into water and titrated with N/IO HCl using methyl red as indicator.

The results are summarised in table II in which w and x have the same significance as in table I and t represents the time in hours.

TABLE II.

	unsub	o isomer	m isomer	p isomer
w	0.453 gm.	0.50I gm.	0.506 gm.	0.500 gm.
t	x	x	x	x
½	55.6	37.9	45.2	45.6
I	68.I	54.4	63.I	56.0
2	8I.2	68.5	75.3	7I.2
4	89.4	8I.9	86.0	83.3
6	93.4	84.7	90.4	86.8

x was graphed against t and this is shown in graph I in the introduction.

Hydrolysis of P methoxy β phenyl ethyl bromide.

P methoxy β phenyl ethyl bromide was hydrolysed under the same conditions as the isomeric tolyl derivatives. The percentage hydrolysed was calculated on the basis of 94% purity i.e. 94% of the weight taken was p methoxy β phenyl ethyl bromide.

The results are given in the following table in/

in which w, x and t have the same significance as in table II.

TABLE III.

p methoxy β phenyl ethyl bromide
w 0.530 gm.

t	x
½	33.3
I	50.4
2	65.7
4	80.I
6	85.0

x was graphed against t in graph II in the introduction and for comparative purposes the hydrolysis curves for β phenyl ethyl bromide and β p. tolyl ethyl bromide were repeated.

Non Reactivity towards Hydrogen Iodide.

A single quantitative investigation of each compound was carried out.

Approximately 0.I gram of β phenyl ethyl bromide and the isomeric β tolyl ethyl bromides were weighed into 25 c.c. standard flasks, I0 c.c. of constant boiling HI added and 5 c.c. of glacial acetic acid. The flasks were heated for four hours in a glycerol thermostat at I00° C, poured into 50 c.c. of water and titrated with 0.083I N $Na_2S_2O_3$ using starch as indicator.

The results are tabulated below. A blank experiment gave a titration of 2.50 c.c.

Compound/

Compound	Weight used	Titration	Titration -blank.
β phenyl ethyl bromide	0.094 gm.	3.04 c.c.	0.54 c.c.
β o tolyl ethyl bromide	0.103	3.05	0.55
β m tolyl ethyl bromide	0.096	2.93	0.43
β p tolyl ethyl bromide	0.099	2.71	0.21

The amount of reactivity towards HI, as represented by the final Column, which is the number of c.c.'s of $Na_2S_2O_3$ equivalent to the amount of iodine liberated, is negligible. This result was anticipated from theoretical considerations.

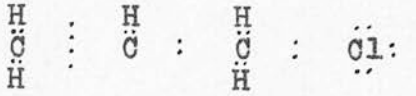
DISCUSSION.

In order to correlate this work with the various recent theories based on the Thomson & Lewis Langmuir theory of the atom (Thomson, Silliman Lectures 1903);(Lewis, J.Amer.Chem.Soc. 1916 38 763)(Langmuir ibid, 1919 41 868 etc.) it is necessary first of all to stress certain features of that theory particularly as applied by Kermack and Robinson (J.1922 121 428). A completely satisfactory interpretation of the theory is still remote, but sufficient has been elucidated by recent investigations to justify a theoretical expression of the result of this research on an electron basis.

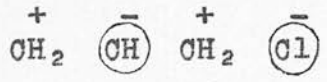
The outstanding feature of the Thomson and Lewis Langmuir theory is the explanation of the nature of chemical combination and the recognition of the tendency to form stable octets in the case of these elements(except hydrogen) which commonly occur in carbon compounds. The positive nature of hydrogen implies that the stable condition is reached when no electrons surround the nucleus. An atom is negative which is surrounded by a stable octet or which tends to attract electrons so as to form a stable octet. The less the electrons are shared by other atoms the more stable is the/

the octet. An important point to note is that a disintegrated octet tends to further disruption.

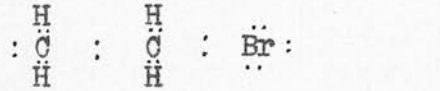
Let us consider firstly a chain of carbon atoms terminated by a halogen atom as in allyl chloride (cf. Kermack and Robinson loc.cit.).



The stable octets formed round the chlorine atom tends to produce an unstable system about the adjacent carbon atom, and the stable system in the second carbon atom is facilitated by the instability of the first carbon atom octet. Thus we can express the compound in terms of positive and negative polarity –



In the same manner the side chain in the isomeric β tolyl ethyl bromides, that is, $-CH_2CH_2Br$



will show a tendency for halogen to complete its octet. This will produce an instability of the carbon octet in proximity to it with the subsequent stabilising of the second carbon octet.

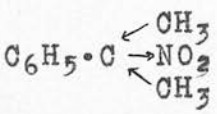
The halogens are recognised from the stability of their ions and other evidences to be elements of high electron affinity and thus there is a tendency to produce a negative charge on the Br atom.

But/

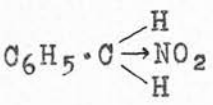
But as shown above there is a compensating movement of electrons through the side chain so that the side chain as a whole will act as an influence tending to thrust electrons into the benzene nucleus.

Alkyl groups contain no unshared electrons and there is a tendency for the repulsion of electrons from an alkyl group.

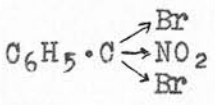
Baker and Ingold (J.1926 2462) have shown the contrast between the high affinity of the halogens and the repulsion of electrons by alkyl groups by substituting CH_3 and Br groups in place of the hydrogen atoms in the rather strongly meta orientating group - CH_2NO_2 , and examining the increase or decrease in the percentage of meta compound obtained on nitration. The compounds examined and the results obtained are given as follows:-



29%



50%



84%

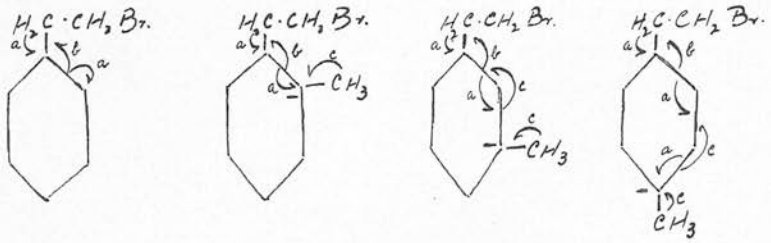
The stability or instability of the carbon octet causes a shift of electrons throughout the whole molecule (Robinson and his collaborators I926; this view shared later by Ingold and his collaborators 1926). For example in the toluene molecule substitution is caused by an electron shift represented by

The ortho and para positions acquire negative charges and/

and thus become positions of attack on further substitution in the benzene molecule. Thus it to be expected that differences in electronic disturbances are responsible for all differences in reactivity in the molecules under discussion.

These may be grouped as follows- 1) disturbances due to the CH_2CH_2Br grouping (a); 2) Disturbances due to the phenyl group (b); 3) disturbances due to the methyl group (c). In the present case there is also a damping effect of general reactivity (d) in the CH_2CH_2Br grouping as opposed to the $CH_2 \cdot Br$ grouping.

This damping effect (d) is measured by the difference between the reactivity of benzyl bromide and β phenylethyl bromide, and is so great as to prevent the differences in reactivity from making themselves very pronounced. The figures representing all the electron disturbances in β phenyl ethyl bromide and the β tolyl ethyl bromides are as follows:-



The effects in each case are summarised in the following.

(c) is an electronic disturbance due to the repulsing electron force set up by the CH_3 group which tends to increase the differences in reactivity while (a), an/

an electron disturbance due to the CH_2CH_2Br group, tends to neutralise disturbances due to the CH_3 group as far as possible. In the ortho and para compounds the CH_3 group is attached to a benzene carbon atom which is the one attacked in substitution and therefore the one which most readily acquires a negative charge. Hence transmission of electrons from the CH_3 group in these positions is prevented and will not take place so readily as in the meta position where the CH_3 group is opposed by a disturbance whose effect is not felt to the full at this point. Thus in the meta position the CH_3 group producing an electronic disturbance (c) tends to eliminate differences in reactivity and promote the normal electronic state at this particular point in the molecule.

The effect of the downward thrust of the CH_2CH_2Br grouping must be great, and it is therefore surprising that there is no greater difference between the ortho and para, and meta isomerides than the figures indicate but the effect is lost on account of the influence (d), the general damping effect, which is very pronounced in the tolyl ethyl bromide molecule.

The marked difference between the β tolyl ethyl bromides and the ω brom xylenes is due to a two fold reason. a) The weaker downward thrust $-CH_2Br$ should be less powerfully ortho and para directing than the CH_2CH_2Br grouping. (This is substantiated particularly by Ingold and his collaborators J.1926). b) The absence of the

damping/

damping effect (d) which gives freedom to all the influences in the molecule.

There is however great difficulty in explaining why the substitution of a CH_3 group should increase the reactivity of a compound containing a CH_2Br group i.e.  and diminish the reactivity of one containing a CH_2CH_2Br group.

SUMMARY.

It has previously been established that induced alternate polarity effects can be detected over a limited number of single bonds eg. in the ω brom xylenes. In this investigation it has been proved that if the same influences are passed through an extra single bond in the β tolyl ethyl bromides the differences in the reactivity of the isomerides almost entirely disappear.

This is shown by a) the lower reactivity of the terminal Br atom towards hydrolysing and reducing agents i.e. there is an appreciable loss in general effect, and b) there is only a slight residuum of alternate polar effect observed.

The steric effect is also present in the tolyl ethyl bromides but to a less pronounced extent. This is evidenced by the slow rate of hydrolysis of the ortho isomer in comparison with the para isomer.

This remarkable loss of reactivity as the number of single bonds is increased is explained on the basis of modern electronic structure.

A partial confirmation of the results of the β tolyl ethyl bromide series was obtained by the examination of p methoxy β phenyl ethyl bromide.

It is also shown that β phenyl ethyl bromide is more reactive towards hydrolysing agents than the substituted derivatives.

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2. The Influence of Substituent Groups on the Course of Etard's Reaction.

Chromyl chloride, which was discovered by Berzelius, was first used as an oxidising agent in organic chemistry by Etard in 1881 whose results were published in the Annales de Chimie et de Physique [5th] 22 218 - 286.

As is well known chromyl chloride reacts with an aromatic hydrocarbon to give a hygroscopic amorphous intermediate compound, which on hydrolysis yields an aldehyde. The method is not generally recognised as a good one for the preparation of aldehydes but occasionally it has proved useful. The influence of the groups present in the reactant molecule on the course of the reaction and on the yield obtained has not been seriously investigated so far. Preliminary observations showed that the nature and position of the groups have a remarkable effect, at least on the formation of the intermediate compound and possibly on the products of hydrolysis.

In a series of oxidations of various nitro toluene derivatives to the corresponding aldehydes using chromyl chloride as an oxidising agent, carried out in these laboratories it was observed that in one case hydrolysis of the intermediate compound produced no aldehyde and an appreciable quantity of the original substance./

substance. The compounds examined were o nitro toluene, 2:4 dinitro toluene and o nitro p methoxy toluene. They each yielded an intermediate compound with varying degrees of ease but on hydrolysis the results were as follows:-

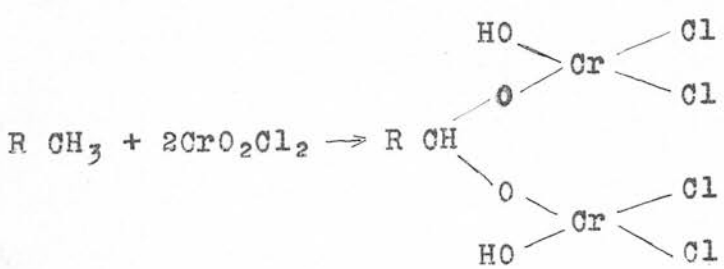
Solid from o nitro toluene - an appreciable quantity of o nitro toluene and no aldehyde.

Solid from 2:4 dinitro toluene - no aldehyde.

Solid o nitro p methoxy toluene - a 50% yield of o nitro p methoxy benzaldehyde.

Henderson and Campbell (J. 1890 57 253) have observed a peculiartity of this nature on the oxidation of nitro benzene with chromyl chloride and their work will be referred to later.

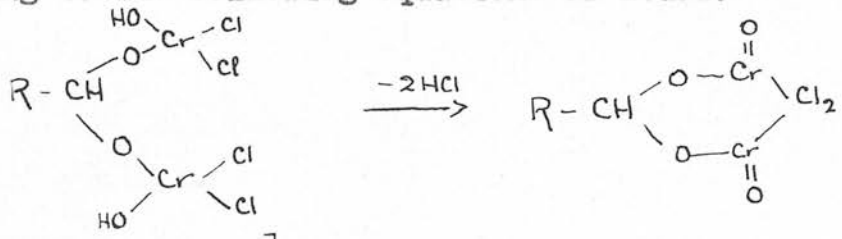
The following research was undertaken in order to investigate this phenomenon and in general to obtain some knowledge of the influence exerted by various substituent groups on the course of Etard's reaction. According to Etard (loc.cit) the mechanism of the reaction is as follows:-

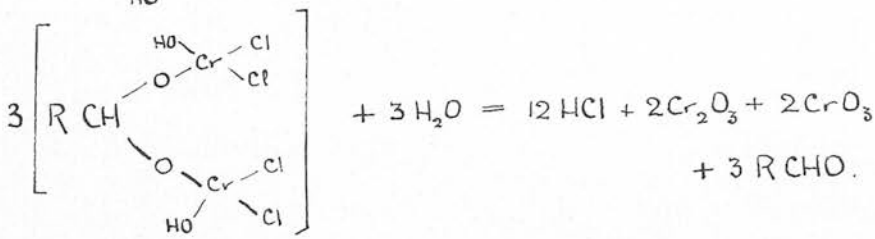


It is seen that he regards the hydrogen of the methyl group as being removed from the hydrocarbon residue/

residue and appearing linked to the oxygen attached to the chromium. Hence it may be expected that general and perhaps alternate polar influences affecting the reactivity of these two hydrogen atoms or the carbon atom of the CH_3 group would make themselves apparent in the rate at which reaction would take place between chromyl chloride and the reactant benzenoid derivatives, i.e. on the rate of formation of the intermediate compound.

Decomposition of these intermediates may be affected in two ways - a) heating, and b) hydrolysis, according to the following equations of Etard.

a) 

b) 

In the following investigation the influence of three substituent groups, the nitro, methoxyl and methyl groups are studied. Compounds were prepared in which these groups were in certain relative positions to each other and also oxidations were attempted on compounds in which either the methoxyl group or the nitro group were absent. The intermediate compounds prepared from these substances were analysed. Two of them were subjected/

subjected to the action of heat and a quantitative estimate was made of the hydrogen chloride evolved. All the intermediate compounds were hydrolysed and the products of hydrolysis isolated.

Several general observations were made as follows with carbon tetrachloride as solvent. a) Compounds containing a nitro group in the molecule form an intermediate compound with chromyl chloride very slowly; b) compounds containing a second methyl group react more quickly; c) methoxy compounds react very rapidly; and d) compounds containing both a nitro group and a methoxyl group are intermediate in reactivity.

This is, as will be seen, paralleled with well known phenomena in other branches of "reactivity investigations". Definite indications of alternating effects in reactivity were observed particularly in the meta and para tolyl methyl ethers.

The intermediate compounds are very reactive towards hydrolysing agents and the action was so rapid in all cases that no differences in the rates of hydrolysis due to substituted groups could be detected.

The stabilising influence of the nitro group and the entirely opposite effect of the methoxyl group extends also to the decomposition by heat of such compounds.

Preparative.

Chromyl chloride.

This preparation involved the following reaction:-

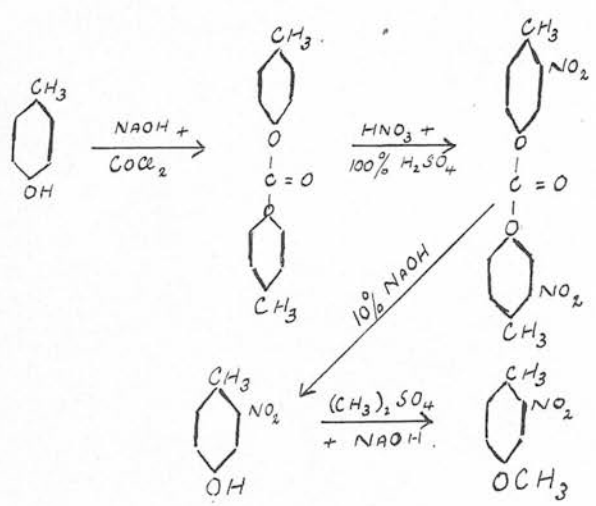
$K_2Cr_2O_7 + 4NaCl + 3H_2SO_4 = K_2SO_4 + 2Na_2SO_4 + 3H_2O + 2CrO_2Cl_2$

Firstly 30 grams of potassium dichromate and 54 grams of sodium chloride were powdered together and fused in an iron still for two hours. This preliminary fusion prevented frothing on the addition of concentrated H_2SO_4 The fused mass was transferred to a retort and 150 c.c. of concentrated H_2SO_4 were added. Fumes of chromyl chloride and hydrogen chloride were evolved. Chromyl chloride was distilled from the reaction mixture and it was then redistilled at 115°-118° C.

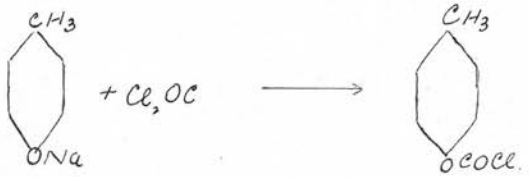
The boiling point of pure chromyl chloride is 117° C.

O nitro p methoxy toluene.

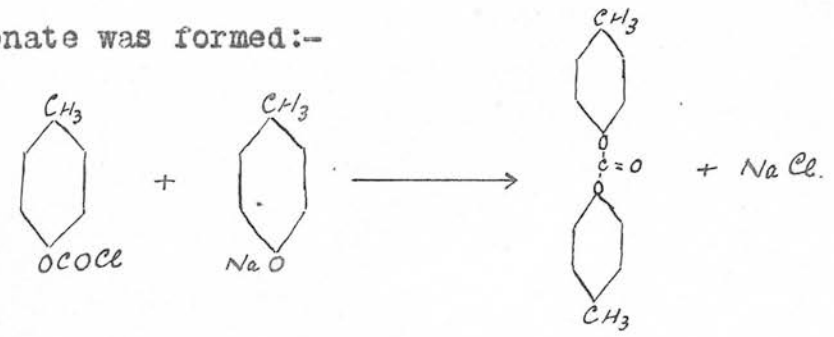
This was prepared according to the following scheme:-



I) One hundred grams p.cresol were dissolved in one molecular proportion of 10% NaOH and phosgene was passed through the solution until no further heat of reaction was generated. The white solid carbonate was produced in quantity in admixture with a yellow oil which has the following constitution.



This intermediate compound in the formation of the carbonate was separated from it and treated with a molecular proportion of sodium cresylate when the solid carbonate was formed:-



The carbonate was recrystallised from alcohol giving a yield of 75 grams. The melting point was not taken.

2) The nitration of the carbonate was carried out according to a method of Holleman (Rec.trav.Chim.1917 36 271) in which a mixture of concentrated HNO_3 and 100 % H_2SO_4 is used as a nitrating agent. It is important that 100% H_2SO_4 is employed and a mixture of 1.5 parts of fuming H_2SO_4 to 1 part of concentrated H_2SO_4 was found to be the most efficient. The nitrated carbonate was hydrolysed/

hydrolysed by boiling it with 10% NaOH for one hour and the product steam distilled to remove m.nitro cresol which is volatile in steam. The residue solidified giving a solid which melted at 76° C. The yield was 30% of the theoretical.

3) The following method of methylating nitro cresol was adopted from Haworth and Lapworth (J. 1923 123 2986) @ nitro cresol was methylated in xylene solution by refluxing for 4 hours with dimethyl sulphate and anhydrous potassium carbonate in order to remove the sulphuric acid formed. The product was steam distilled and the xylene which distilled first was collected separately. The distillate was extracted, dried and distilled and o nitro p methoxy toluene came over as a yellowish liquid at 256° - 260° C.

M Tolyl methyl ether.

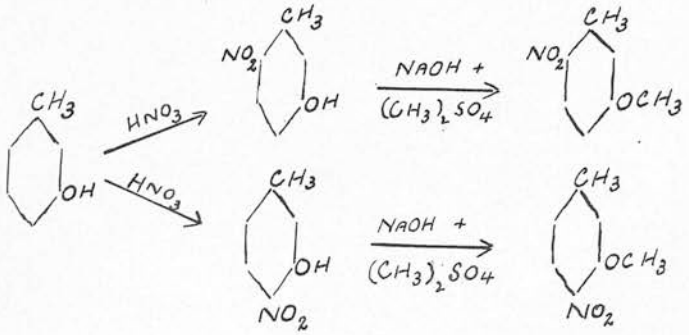
Forty eight grams of m cresol were methylated by admixture with 9 grams of NaOH in 65 c.c. of water and 25 grams of dimethyl sulphate added. The whole was shaken for 15 minutes, 10 grams more NaOH were added and the mixture refluxed for 7 hours. A liquid separated partially from the aqueous layer and it was extracted, washed with water, dried and fractionally distilled. The m tolyl methyl ether distilled at 173°-176° C.(correct B.P. = 175°-176° C) and the yield was 30 grams which was 60% of the theoretical.

3 methoxy/

3 methoxy 4 nitro toluene

and 3 methoxy 6 nitro toluene

These compounds were prepared according to the following scheme:-



This method of preparation is due to Haworth and Lapworth (J.1923 123 2986) who used Staedel's method of nitrating m.cresol (Ann. 1883 217 49; 1890 259 208). M cresol in solution in glacial acetic acid was cooled to -5° C. and a mixture of fuming HNO_3 (D 1.5) and glacial acetic acid cooled to -15° C. was slowly added during 1½ hours. The temperature of the reaction mixture was not allowed to rise above -1° C. The reddish brown mass was poured on to excess of ice. A mixture of 3 hydroxy-4 nitro toluene and 3 hydroxy 6 nitro toluene crystallised out and the two compounds were separated by steam distillation since the 1,3 6 compound is non volatile in steam and the 1,3 4 compound is volatile in steam.

From 35 grams of m.cresol there were obtained 10 grams/

grams of I,3,6 compound with a melting point of I20°-I24° C. and 6 grams of I,3,4 compound with a melting point of 54° C.

The methylation of the above compounds was carried out as in the methylation of o nitro cresol (Haworth and Lapworth loc.cit.). At the completion of the reaction which took I8-24 hours the mixture was diluted with dilute alkali and steam distilled. As before the xylene was collected separately. The nitro tolyl ether solidified in the distillate and was recrystallised from 96% alcohol.

The melting points of the compounds are as follows:-

3 methoxy 4 nitro toluene 59° C.(Gibson J.1923 123 1269 M.p. = 62° C)
(Haworth & Lapworth loc.cit. M.p. = 60°-6I° C.)

3 methoxy 6 nitro toluene 52° C (Gibson=53° C)
(Haworth & Lapworth = 54°-55° C.)

Preparation of the Intermediate Compounds in the Oxidation of aromatic hydrocarbons by chromyl chloride.

The intermediate compound is of a very hygroscopic nature and precautions were therefore necessary in its preparation to prevent partial hydrolysis by atmospheric moisture.

In the general method given below it will be observed that one solvent was used throughout thus ensuring that the temperature of the reaction mixture did/

didnot at any time exceed a maximum i.e. the boiling of the solvent 76° C.

The standardisation of temperature, was necessary for two reasons:-

I) Etard in his original work, as has already been stated, observed that at a definite temperature varying for each compound, the intermediate compound loses two molecules of hydrogen chloride quantitatively according to the equation

$$R\,CH_3 \;2\;CrO_2Cl_2 \xrightarrow{-2HCl} R\,CH.2CrO_2Cl$$

He prepared his intermediate compounds over a wide range of temperature with and without a solvent and the constitution of the resulting compound was either of the one general formula or the other according to the conditions of the experiment. But in the present research the conditions were standardised in order that the constitution of the intermediate compounds would all be of the one form. A temperature of reaction far below the lowest decomposition temperature recorded by Etard ensured that the possibility of formation of the type of compound R CH.2CrO_2Cl was remote.

2) It was desired to indicate the order of reactivity of various compounds by observing the comparative rates at which the intermediate compounds were produced and this comparison was only possible at an approximately constant temperature.

Intermediate/

Intermediate Compound.

A 10% solution of each initial substance in carbon tetrachloride was stirred mechanically during the slow addition of two molecular proportions of chromyl chloride. All reagents were carefully dried. The readiness of formation of the intermediate compound determined the length of time the mixture was heated on the water bath, periods varying from 15 minutes to an hour in most cases. The chocolate brown intermediate compound was filtered and washed very carefully with carbon tetrachloride in order to remove any unchanged initial compounds. It was then transferred to a vacuum dessicator and dried over phosphorus pentoxide. These operations were carried out as quickly as possible.

After the bulk of the carbon tetrachloride adhering to the compound had been removed it was transferred to a flask containing a layer of phosphorus pentoxide and the flask heated on a water bath with simultaneous evacuation. This operation removed the final traces of carbon tetrachloride. Carbon tetrachloride was replaced by carbon disulphide as a solvent in the formation of the intermediate compounds but certain of the compounds were slow in forming and the yields obtained were poor at the lower temperature (i.e. 61°, the boiling point of CS_2) so carbon tetrachloride was retained.

It was observed, in the case of the intermediate compound/

compound from o nitro toluene at least, that on opening the flask an odour resembling phosgene was observed.

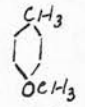
According to Etard there is a reaction between carbon tetrachloride and chromyl chloride although the statement is refuted by Moles and Gomez (Anales Soc. españ fis quim 1914 12 142-54) who successfully carried out ebullioscopic studies of chromyl chloride in carbon tetrachloride solution.

In order to determine if the odour was due to phosgene as a product of the interaction of carbon tetrachloride and chromyl chloride the gases from the evacuation of the flask were drawn through a sodium phenolate solution which would indicate the presence of phosgene by the formation of white solid phenol carbonate. This test gave negative results. A silver nitrate solution was substituted but only a slight turbidity was detected during two hours.

If any reaction did take place between chromyl chloride and the solvent, carbon tetrachloride, under the conditions of the experiment, the resulting compounds were not isolated or identified. It was also proved from the above test with silver nitrate solution that carbon tetrachloride was almost completely removed from the intermediate compound.

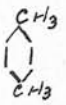
It was possible by observation of the rate of formation of the intermediate compounds and the yields obtained to give an indication of the order of reactivity of/

of the initial compounds. The order is from the most reactive p tolyl methylether to the least reactive 2:4 dinitro toluene.

p tolyl methyl ether 

anisole 

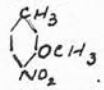
m tolyl methyl ether 

p xylene 

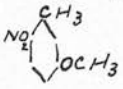
o nitro p methoxy toluene 

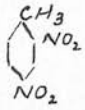
a nitro toluene 

m nitro toluene 

3 methoxy 4 nitro toluene 

} practically equal in reactivity

3 methoxy 6 nitro toluene 

2:4 dinitro toluene 

An account of any abnormality in the preparation of the intermediate compounds of these substances is now given.

<u>Intermediate compound of p tolyl methyl ether</u>.

It was formed with explosive violence below 0° C. The addition of each drop of chromyl chloride to the well cooled solution caused a vigorous local action with the immediate formation of a dark brown solid which on drying turned purple in colour.

<u>Intermediate/</u>

Intermediate Compound of Anisole.

There were two deviations from the general character of the reaction inthis case,

I) The colour of the reaction mixture on the addition of chromyl chloride turned green.

2) There was an appreciable heat of reaction.

Intermediate Compound of 2:4 dinitro toluene.

It was only formed in very slight quantity after refluxing for several hours.

EXPERIMENTAL.

Analysis

Chromium and chlorine were estimated in each intermediate compound.

The very hygroscopic nature of these compounds necessitated precautions being taken particularly in weighing quantities for analysis. The compounds were kept in vacuum dessicators over phosphorus pentoxide in a partial vacuum. A weighing bottle with an accurately fitting stopper was used and the whole operation was carried out as quickly as possible concomitant with accuracy.

Estimation of Chlorine.

Chlorine was estimated by the method of Carius i.e. a weighed quantity of the compound was heated to about 200° C in a sealed tube with silver nitrate and concentrated HNO_3 and the resulting silver chloride filtered, dried and weighed in the usual manner.

Estimation of Chromium.

There is no reference in Etard's original work to the actual method of procedure adopted in his estimation of chromium.

Two methods were evolved.

About 0.5 gram of the intermediate compound to be analysed was weighed out and transferred to a flask with about 200 c.c. of water and hydrolysed by heating it to 60°/

60° for an hour. The chromium was now present in solution in the chromate and chromic state. The solution was filtered and extracted with ether to remove the organic products of hydrolysis. The aqueous layer was accurately separated off and the ether in solution was removed by evaporation. The solution was then made up to a known volume (usually 250 c.c) in a standard flask.

Gravimetric method. The chromium was weighed as Cr_2O_3.

The chromium in a known volume of the above standard solution was reduced to the chromic state by the addition of 10 c.c. of freshly prepared sulphurous acid, the solution being boiled for one minute.

Ammonium sulphide had previously been prepared in the usual way by saturating a known volume of NH_4OH (D.880) with H_2S and adding to it an equal volume of the ammonia. This freshly prepared ammonium sulphide solution was added drop by drop to the boiling solution. Chromic hydroxide was precipitated, coagulated and filtered, and incinerated strongly for 30 minutes. The chromium was then weighed as chromic oxide Cr_2O_3.

An attempted estimation of the chlorine in the compound, which was contained in the filtrate by adding a known volume of standard silver nitrate to precipitate silver chloride, failed. A slight quantity of organic matter was filtered with the silver chloride and

partially/

partially reduced the silver chloride to metallic silver. No further work was done on this method of estimating chlorine as it was obviously inaccurate.

Volumetric method.

The chromium was estimated volumetrically by converting it to dichromate by oxidation with potassium permanganate. The dichromate liberated iodine from potassium iodide according to the equation

$K_2 Cr_2 O_7 + 6KI + I4\ HCl = 8KCl + 2Cr\ Cl_3 + 6I + 7H_2O$

The iodine liberated was titrated with sodium thiosulphate in the usual way.

As the method was original it was tested in the following manner:-

20 c.c. of N/10 $K_2Cr_2O_7$ were reduced with SO_2 in the cold and the product evaporated to dryness on the water bath. It was then diluted and boiled with 25 cc. dilute H_2SO_4 and 25 c.c. N/10 $KMnO_4$ slowly added to the boiling solution.

The solution was boiled for three minutes and heated on the steam bath for one hour to cause coagulation of the manganese dioxide formed. The precipitate was filtered and washed with water and a solution of two grams of potassium iodide in 10 c.c. of water was added to the filtrate and the liberated iodine was titrated with .0991 N $Na_2S_2O_3$. The titration was 20.17 c.c.

The iodine liberated by 20 c.c. of the original solution/

solution of $K_2Cr_2O_7$ was directly titrated with $Na_2S_2O_3$ and the titration was 20.34 c.c.

The error in this method was therefore not of any great magnitude.

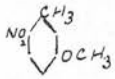
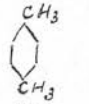
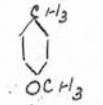
The above method was used without any modification in analysing the original chromium solution of the hydrolysed intermediate compound.

A summary of the results obtained for chlorine and chromium is given below.

No accurate results were obtainable for 2:4 dinitro toluene probably owing to the long period of heating necessary to form the intermediate compound resulting in secondary reactions taking place.

Table/

Table.

Compound		Theoretical Percentage of Chlorine & Chromium			Experimental results.		
		Formulae of intermediate compound.	Cl.	Cr.	Cl.	Cr. Gravimetric	Cr. Volumetric
o nitro toluene		$C_6H_4NO_3CH_32CrO_2Cl_2$	31·8	23·3	31·2	23·2	23·1
m nitro toluene		$C_6H_4NO_2CH_32CrO_2Cl_2$	31·8	23·3	32·7	24·6	–
o nitro p methoxy toluene		$C_6H_3(NO_2)OCH_3CH_32CrO_2Cl_2$ $C_6H_3(NO_2)OCH_3CH_34CrO_2Cl_2$	29·8 36·1	21·8 26·4	33·5	23·9	23·1
3 methoxy 4 nitro toluene		$C_6H_3(NO_2)OCH_3CH_32CrO_2Cl_2$ $C_6H_3(NO_2)OCH_3CH_34CrO_2Cl_2$	29·8 36·1	21·8 26·4	31·2	23·3	–
3 methoxy 6 nitro toluene		$C_6H_3(NO_2)OCH_3CH_32CrO_2Cl_2$ $C_6H_3(NO_2)OCH_3CH_34CrO_2Cl_2$	29·8 36·1	21·8 26·4	29·7	23·7	23·2
p xylene		$C_6H_4(CH_3)_32CrO_2Cl_2$ $C_6H_4(CH_3)_24CrO_2Cl_2$	34·1 39·1	25·0 28·7	38·3	25·4	–
p tolyl methyl ether.		$C_6H_4OCH_3CH_32CrO_2Cl_2$ $C_6H_4OCH_3CH_34CrO_2Cl_2$	32·9 39·3	24·1 28·0	39·5	20·7	–

It may be stated here that none of the intermediate compounds examined have analysis figures which agree with those of a compound of the general formula R CH. $2CrO_2Cl$.

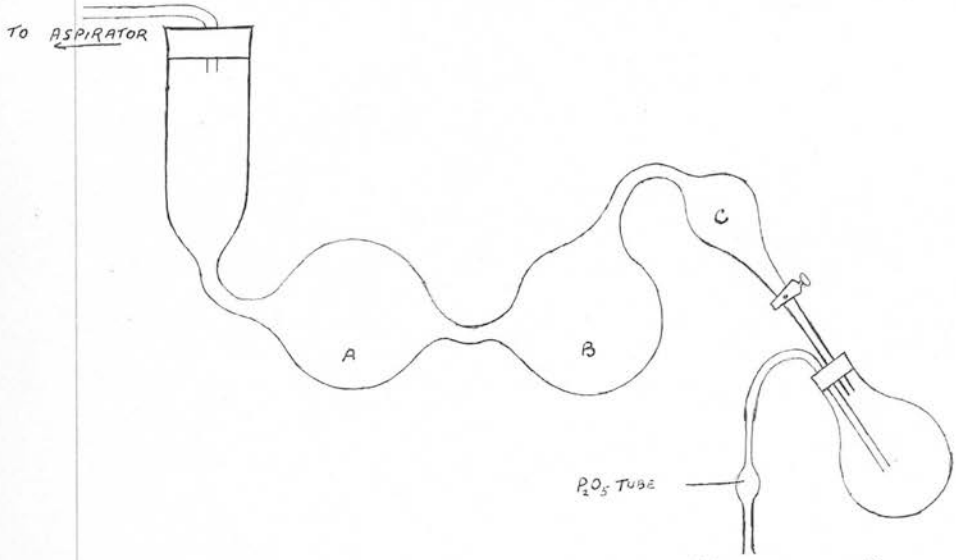
Decomposition.

As already stated Etard observed that the substances he examined with the general formula R CH_3 $2CrO_2Cl_2$ on heating above a specified temperature evolved two molecules of hydrogen chloride quantitatively giving a compound of the nature R CH. $2CrO_2Cl$.

Experiments were performed to see if a quantitative examination of the reaction could be obtained

$$R\ CH_3\ 2CrO_2Cl_2 \longrightarrow R\ CH.\ 2CrO_2Cl + 2HCl$$

The following apparatus was designed:-



O nitro toluene and o nitro p methoxy toluene intermediate compounds were examined. A small quantity (0.2 - 0.3 gram) of the intermediate compound was weighed in the flask and 20 c.c. of N/10 $AgNO_3$ were placed in each absorption bulb A and B. Bulb C acted as /

as a trap to catch any organic matter carried up the tube. A slow current of dry air was aspirated through the apparatus and the flask was heated on an oil bath. The temperature at which a precipitate was first observed in the absorption bulbs was noted as being the decomposition temperature of the intermediate compound. The flask was kept at a temperature 20° higher than the decomposition temperature for one hour.

The contents of the absorption bulbs were washed into a basin and the excess $AgNO_3$ back titrated with potassium thiocyanate using ferric indicator.

Results:-

Decomposition temperature of the intermediate Compounds of o nitro toluene = 295° C.

o nitro p methoxy toluene = 142° C.

The theoretical percentage of HCl was based on the formula R $CH_3 2CrO_2Cl_2$.

O nitro toluene % of HCl obtained = 15.0%

$NO_2C_6H_4CH_3.2CrO_2Cl_2$ requires 16.3%

O nitro p methoxy toluene % of HCl obtained = 8.3%

$NO_2C_6H_4OCH_3CH_3 2CrO_2Cl_2$ requires 15.3%

HYDROLYSIS.

Three methods of hydrolysis were tried.

I) The intermediate compound was heated to 50°-60° C. for one hour with IO times its weight of water.

The product of certain of the hydrolyses were acids and not aldehydes as anticipated. It was thought that in these cases chromic acid as a product of the hydrolyses was oxidising any aldehyde formed, to acid.

So a modification was introduced.

2) The intermediate compound in IO times its weight of water was stirred in a flask carrying a mercury sealed stirrer. A slow current of SO_2 was passed in and the mixture heated simultaneously to 60° C. The whole operation took 30 minutes. This modification was introduced so that chromic acid in an atmosphere of SO_2 would not oxidise aromatic aldehydes to acids.

3) Finally the intermediate compound in aqueous solution was stirred at room temperature for one hour.

The intermediate compound from o nitro toluene was hydrolysed by each method and the products of hydrolysis were the same in each case.

The method finally adopted was the second one.

There is given below a tabulation of the products of the hydrolysis of each compound and an account of the methods of isolating and detecting the products.

o nitro/

o nitro toluene -	50% yield of o nitro benzoic acid; an appreciable quantity of o nitro toluene; and a trace of an aldehyde.
m nitro toluene -	m nitro benzoic acid
o nitro p methoxy toluene -	mainly o nitro p methoxy benzoic acid; a slight quantity of o nitro p methoxy benzaldehyde.
3 methoxy 4 nitro toluene -	mainly 3 methoxy 4 nitro benzoic ac id; 3 methoxy 4 nitro toluene and a trace of an aldehyde.
p tolyl methyl ether -	anisaldehyde
m tolyl methyl ether -	trace of an aldehyde
p xylene -	trace of an aldehyde
anisole -	I:4 quinone

<u>O nitro toluene.</u>

The hydrolysed solution was extracted with ether and the ethereal layer extracted with alkali. The ethereal layer on removal of ether gave a yellow semi-solid. A trace of a p nitro phenyl hydrazone was formed but no aldehyde could be isolated with sodium bisulphite solution. A trace of a compound containing hydrolysable/

hydrolysable chlorine was also detected.

The main product of the ethereal layer was o nitro toluene with a boiling point of 217°C (correct B.P. 222°C). The alkaline extract on acidification gave o nitro benzoic acid which on recrystallisation from 60°-80° petrol ether gave a melting point of 141°C. (correct M.P. = 147°C).

m nitro toluene

The products of hydrolysis were extracted in the same manner.

The ethereal layer gave no trace of aldehyde but a red oil in insufficient quantity to investigate. It was possibly unchanged m nitro toluene.

The alkaline extract on acidification gave a yellow solid with a melting point of 137°C. (correct M.P. of m nitro benzoic acid = 140°C.).

o nitro p methoxy toluene.

The ethereal extract yielded a yellow solid which gave a p nitro phenyl hydrazone with a melting point of 246°C. On dissolving the solid in ether and extracting with alkali and acidifying, a solid was obtained which melted at 197°C. [M.P. of o nitro p methoxy benzoic acid = 195° - 196° (Simonsen and Rau J. 1917 III 236)]

A small quantity of o nitro p methoxy benzaldehyde was isolated which melted at 96°C and on analysis it contained 7.94% N_2

$C_8H_7NO_4$ requires 7.74% N_2.

3 methoxy 4 nitro toluene.

The ethereal extract gave a yellow crystalline solid which was dissolved in ether and extracted with alkali. The alkaline extract on acidifying yielded a yellow solid which on recrystallisation from benzene melted at 210° - 212° C.

(M.P. of 3 methoxy 4 nitro benzoic acid = 208° C.

Rieche Ber., 1889 22 2363)

The ethereal layer gave a yellow solid which on recrystallisation from water melted at 53° - 54° C. (M.P. of 3 methoxy 4 nitro toluene = 60° - 61° C.).

A trace of an aldehyde was observed.

P tolyl methyl ether.

The ethereal extract gave a red oil having a strong odour of anisaldehyde from which a p. nitro phenyl hydrazone was prepared. This derivative presented some difficulty on recrystallisation and in consequence the melting point of 208° C was not in good agreement with anisaldehyde p nitro phenyl hydrazone (M.P. = 220° C)

m tolyl methyl ether

A red oil was obtained from the ethereal extract which gave a trace of a p nitro phenyl hydrazone but nothing further could be determined. This also was the result of an investigation of p xylene.

Anisole.

The results of the hydrolysis proved to be very/

very interesting. The ether extract yielded a red liquid which solidified to a dark coloured solid with a quinone odour. On the upper portion of the flask yellow crystals had sublimed.

The solid was steam distilled and the distillate gave a yellow crystalline solid with a melting point of 109°C. (M.P. of 1.4 quinone = 116°C.) The residue from steam distillation was again steam distilled with a little ferric chloride when a further quantity of a yellow solid was produced.

To prove its constitution it was suspended in water and SO_2 passed through. The colourless solution produced, yielded, on extraction with ether, a white solid which on recrystallisation from benzene gave a melting point of 171°C (M.P. of 1.4 hydroquinone = 169°C) The following test substantiated the proof of its constitution. An aqueous solution with neutral ferric chloride solution gave a transient green colouration, and with ammonium hydroxide gave a reddish brown colouration. It was therefore 1.4 hydroquinone and the original product of hydrolysis was 1.4 quinone.

DISCUSSION.

General Remarks.

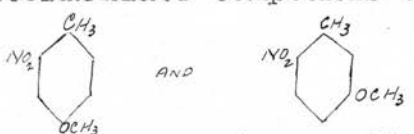
The results of analysis show that in most cases the chromium and chlorine percentages are higher than that demanded by theory. Several investigators have observed this and it is attributed to the difficulty of freeing the amorphous intermediate compound entirely from traces of chromium compounds precipitated with it. It will be observed however that o. nitro toluene and to a lesser extent m. nitro toluene are compounds which agree well with the results anticipated. It has been proved conclusively by the ready formation of an amorphous intermediate compound with anisole and CrO_2Cl_2 that a compound containing a methoxyl group is attacked by chromyl chloride. It is thus possible that secondary reactions are taking place in compounds containing a methoxyl group or a second methyl group which also accounts for the high analysis figures obtained.

An examination of the comparative rates of formation of the intermediate compounds led to some interesting observations.

The presence of a nitro group has a remarkable retarding effect on the rate of formation. For example p tolyl/

p tolyl ethyl ether is the most reactive of the compounds examined but the introduction of a nitro group i.e. o nitro p methoxy toluene, slows down the rate of formation considerably. The compounds containing nitro groups all produce intermediate compounds comparatively slowly. Two nitro groups in the molecule as in 2:4 dinitro toluene almost preclude the formation of the intermediate compound.

Comparison of rates of formation of para and meta tolyl methyl ethers indicates that a methoxyl group in the para position to the methyl group has a much greater accelerating effect on the rate of formation than a methoxyl group in the meta position, an observation confirmed in a comparison of the rate of formation of intermediate compounds of



both of which are retarded in reactivity by a nitro group in the 6 position to the methyl group.

The decomposition temperatures of the intermediate compounds of o nitro toluene and o nitro p methoxy toluene also served to indicate the stabilising effect of a nitro group in the molecule and how this effect is destroyed by the introduction of a methoxyl group.

Of the eight compounds examined two aldehydes were actually isolated, four acids and a quinone. In two/

two cases the initial substance was obtained in quantity.

Henderson and Campbell (J. 1890 57 253) observed in the oxidation of nitro benzene by CrO_2Cl_2 in $CHCl_3$ solution that nitrobenzene was produced from a brown amorphous intermediate compound which corresponded in composition with a formula $C_6H_3(NO_2)(CrO_2Cl)_2$. They suggested that nitroquinone was formed on treating the solid with water which at once decomposed with the regeneration of nitrobenzene. This nitroquinone was not isolated.

In the present investigation the intermediate compounds of o nitro toluene and 3 methoxy 4 nitro toluene, which are the compounds from which initial substances were isolated, both correspond to the general formula $R\,CH_3{}_2CrO_2Cl_2$. Other products of oxidation were isolated which proves that a reaction has taken place and that it is not merely a loose addition compound, which has been formed which completely decomposes again into the hydrocarbon and inorganic chromium compounds. Also the quantities of initial compounds isolated substantiate the explanation that the nitrotoluenes, as has already been observed, do not readily and completely react with CrO_2Cl_2 in CCl_4 solution and the residual nitro toluene is retained by the amorphous intermediate compound even after careful washing and appears along with the products of hydrolysis.

The/

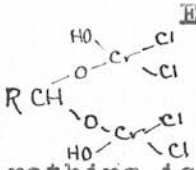
The formation of acids instead of aldehydes on hydrolysis is difficult to explain satisfactorily ※ . The hydrolysis was performed in an atmosphere of SO_2 and spontaneous oxidation of the aldehyde to the corresponding acid after separation is unlikely since in one case i.e. o nitro p methoxy toluene, both aldehyde and the corresponding acid were obtained together. It is possible that hydrolysis and oxidation are so rapid that they take place in the aqueous solution even in presence of SO_2.

Quinone must result from anisole after demethylation and oxidation of the para carbon atom.

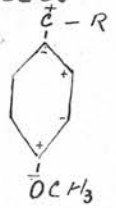
※ Von Richter (Ber. 19 1060) has prepared p. nitro benzoic acid by the oxidation of nitro toluene by chromyl chloride at 160° and Henderson and Campbell (loc.cit.) confirmed his work.

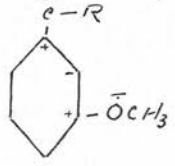
CONCLUSION.

Etard has postulated a linkage of the nature



in the intermediate compound but nothing is known definitely of the structure of the compound. It does not matter materially how the chromium is linked up. The main fact is that oxidation takes place at the moment of formation of the intermediate compound i.e. oxygen is directly united to the carbon atom of the methyl group. The capacity for oxidation depends on the positive nature of the carbon atom. If it is very positive in character it readily takes up the negative oxidiser ($\overline{CrO_2Cl_2}$). It has been shown that a methoxyl group in the molecule activates it appreciably, and that a para substituted methoxyl group induces a much greater "positivity" on the carbon of the side chain than does a meta substituted methoxyl group as is seen here.-





The positively induced carbon atom of the methyl group in the para compound will unite very readily with a negative oxygen atom of the chromyl chloride i.e. the para compound will oxidise more readily/

readily than the meta compound.

The rate of formation of intermediate compounds is completely paralleled by the investigations of Shoesmith and his collaborators on the reactivity of various substituted benzyl bromides.

Confining attention to the investigations on the influence of the methoxyl and nitro groups on the reactivity of the halogen atoms it has been found that a methoxyl group in the para position to a $-CH_2Br$ group renders it very readily hydrolysed and very difficult to reduce, whilst a methoxyl group in the meta position has the reverse effect. Now if the oxidation is the opposite of reduction,(as is very probable through not established with certainty) then an obvious parallel can be drawn in the two series.

P methoxy benzyl bromide is hydrolysed with extraordinary rapidity and p methoxy toluene forms its intermediate compound with CrO_2Cl_2 with explosive violence even in carbon tetrachloride solutions. Meta methoxy benzyl bromide is very much more stable to aqueous alcohol, and meta methoxy toluene froms its intermesiate compound less readily.. P methoxy m nitro benzyl bromide is very much more stable to hydrolysing agents whilst o nitro benzyl bromide is very stable, a phenomenon paralleled by the smooth formation of the intermediate compound from o nitro p methoxy toluene and o nitro toluene itself.

The/

The marked general inhibiting influence of the nitro group and the powerful alternating influence of the methoxyl group have thus proved to be the important factors in the formation of the intermediate compounds.

SUMMARY.

The effect of the introduction of a methoxyl group and a nitro group on various substituted toluene derivatives has been described. The strong inhibiting and stabilising influence, of the nitro group and the activating influence of a methoxyl group on the rate of formation of the intermediate compound and on the products of hydrolysis have been demonstrated and been explained on the basis of a general and alternate polar effect on the carbon atom of the reactant methyl group.

The phenomenon of the recovery of initial substances from oxidations by chromyl chloride has been explained by reference to the strong inhibiting action of the nitro group, which prevents a complete reaction taking place between the initial substance and chromyl chloride.

It has been shown that chromyl chloride forms an intermediate compound with anisole which hydrolyses to give I.4 quinone.